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L8 ANSWER 1 OF 41 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 131:82842 CA
TITLE: Enadoline, a selective .kappa.-opioid receptor **agonist** shows potent antihyperalgesic and antiallodynic actions in a rat model of surgical pain.
AUTHOR(S): Field, Mark John; Carnell, Anthony James; Gonzalez, Maria Isabel; McCleary, Scott; Oles, Ryszard Jan; Smith, Robert; Hughes, John; Singh, Lakhbir
CORPORATE SOURCE: Parke-Davis Neuroscience Research Centre, Department of Biology, Cambridge University Forvie Site, Robinson Way, Cambridge, CB2 2QB, UK
SOURCE: Pain (1999), 80(1,2), 383-389
CODEN: PAINDB; ISSN: 0304-3959
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d kwic

L8 ANSWER 1 OF 41 CA COPYRIGHT 2002 ACS
TI Enadoline, a selective .kappa.-opioid receptor **agonist** shows potent antihyperalgesic and antiallodynic actions in a rat model of surgical pain.
AB Enadoline is a highly selective and potent .kappa.-opioid receptor **agonist**. This report describes and compares the activities of enadoline and morphine in a rat model of postoperative pain. A 1. . . that administration of morphine (1-6 mg/kg, s.c.) 0.5 h before surgery can prevent the development of thermal hyperalgesia with a **MED** of .ltoreq.1 mg/kg, but has little effect on static allodynia. In the present study similar administration of morphine (1-3 mg/kg),. . .
IT Pain
Skin, disease
(allodynia; enadoline, a selective .kappa.-opioid receptor **agonist** shows potent antihyperalgesic and antiallodynic actions in a rat model of surgical pain.)
IT Analgesics
(enadoline, a selective .kappa.-opioid receptor **agonist** shows potent antihyperalgesic and antiallodynic actions in a rat model of surgical pain.)
IT Breathing (animal)
(isoflurane-induced respiratory depression; enadoline, a selective .kappa.-opioid receptor **agonist** shows potent antihyperalgesic and antiallodynic actions in a rat model of surgical pain.)
IT Opioids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.kappa.-; enadoline, a selective .kappa.-opioid receptor **agonist** shows potent antihyperalgesic and antiallodynic actions in a rat model of surgical pain.)

IT 57-27-2, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(comparison; enadoline, a selective .kappa.-opioid receptor **agonist** shows potent antihyperalgesic and antiallodynic actions in a rat model of surgical pain.)
IT 124378-77-4, Enadoline
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enadoline, a selective .kappa.-opioid receptor **agonist** shows potent antihyperalgesic and antiallodynic actions in a rat model of surgical pain.)

=
=> d l13 16 ibib

L13 ANSWER 16 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 132:22957 CA
TITLE: Preparation of spiropiperidine derivatives as **melanocortin** receptor agonists
INVENTOR(S): Nargund, Ravi P.; Ye, Zhixiong; Palucki, Brenda L.; Bakshi, Raman K.; Patchett, Arthur A.; Van Der Ploeg, Leonardus H. T.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

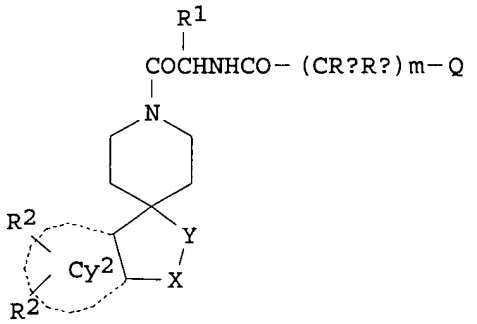
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964002	A1	19991216	WO 1999-US13252	19990610
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9946801	A1	19991230	AU 1999-46801	19990610
AU 742425	B2	20020103		
EP 1085869	A1	20010328	EP 1999-930220	19990610
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
US 6294534	B1	20010925	US 1999-329814	19990610
JP 2002517444	T2	20020618	JP 2000-553071	19990610
US 2001029259	A1	20011011	US 2001-781373	20010212
US 6410548	B2	20020625		

PRIORITY APPLN. INFO.:
US 1998-88908P P 19980611
GB 1998-17179 A 19980806
US 1999-123260P P 19990308
US 1999-329814 A3 19990610
WO 1999-US13252 W 19990610

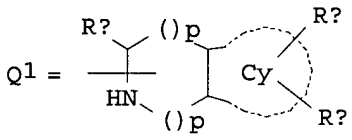
OTHER SOURCE(S): MARPAT 132:22957
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l13 16 abs

L13 ANSWER 16 OF 16 CA COPYRIGHT 2002 ACS
GI



I



AB Certain novel spiropiperidine compds. I [Cy2 = six-membered arom. ring contg. 0 or 1 N; X = O, CH2, etc.; Q = Q1; Y = CO, SO2, etc; R1, Rb = H, C1-8 alkyl, etc.; R2 = H or halo; Rc = Rb, halo, ORb, NHSO2Rb, N(Rb)2, SO2Rb, CF3, OCF3; Cy = aryl, 5 or 6 membered heteroaryl, 5 or 6 membered heterocyclyl, 5 or 6 membered carbocyclyl; m, p, q independently = 0, 1, or 2] are agonists of **melanocortin** receptors (no data) and are useful for the treatment, control or prevention of diseases and disorders responsive to the activation of **melanocortin** receptors. The compds. of the present invention are therefore useful for treatment of diseases and disorders such as obesity, diabetes, **sexual dysfunction** including erectile dysfunction and female **sexual dysfunction**.

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=> d ibib abs kwic 1-16

L20 ANSWER 1 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 137:52344 CA
TITLE: Treatment of male **sexual dysfunction**
INVENTOR(S): Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn; Wayman, Christopher Peter
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 179 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047670	A1	20020620	WO 2001-IB2399	20011210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002028799	A1	20020307	US 2001-895367	20010629
US 2002102707	A1	20020801	US 2001-905846	20010713

PRIORITY APPLN. INFO.:

GB 2000-30647	A	20001215
GB 2001-8730	A	20010406
GB 2001-9910	A	20010423
GB 2001-11037	A	20010504
US 2001-895367	A	20010629
US 2001-905846	A	20010713
GB 2001-20679	A	20010824
GB 2000-16684	A	20000706
GB 2000-17387	A	20000714
US 2000-219100P	P	20000718
US 2000-220908P	P	20000726
US 2001-265358P	P	20010131
GB 2001-6167	A	20010313
GB 2001-8483	A	20010404

AB The use of an inhibitor of a neuropeptide Y (NPY), preferably of a NPY Y1 receptor, which inhibitor is selective for an NPY or NPY Y1 receptor assocd. with male genitalia, in the prepn./manuf. of a medicament for the treatment or prevention of **male erectile dysfunction** (MED).

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Treatment of male **sexual dysfunction**

AB The use of an inhibitor of a neuropeptide Y (NPY), preferably of a NPY Y1 receptor, which inhibitor is selective for an NPY or NPY Y1 receptor assocd. with male genitalia, in the prepn./manuf. of a medicament for the treatment or prevention of **male erectile dysfunction** (MED).

ST male **sexual dysfunction** neuropeptide Y inhibitor sequence

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(5-HT1A, modulators; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(5-HT2A, modulators; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(5-HT3, modulators; neuropeptide Y inhibitors for treatment of male

sexual dysfunction)
IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(5HT6, modulators; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Dopamine agonists
(D2; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Dopamine agonists
(D3; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ORL1, agonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Neuropeptide Y receptors
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Y1; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Bombesin receptors
Endothelin receptors
Gastrin-releasing peptide receptors
Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antiestrogens; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Appetite
(bulimia; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Ion channel blockers
(calcium; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Drug delivery systems
(carriers; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Penis
(corpus cavernosum; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Appetite
(disorder; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Alkaloids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ergot; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Prostaglandins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Sexual behavior
(impotence; neuropeptide Y inhibitors for treatment of male

sexual dysfunction)
IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(intermediate conductance calcium-activated, modulators; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**
)
IT Reproductive organ
(male; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin**, agonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators of, for noradrenaline, dopamine, and serotonin; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Cannabinoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT 5-HT agonists
5-HT antagonists
Anesthesia
Anorexia
Anticholesteremic agents
Anticoagulants
Antidiabetic agents
Antiobesity agents
Blood pressure
Dopamine agonists
Fluorometry
Human
Nervous system agents
Obesity
Opioid antagonists
Platelet aggregation inhibitors
Protein sequences
Purinoceptor agonists
Vasodilators
cDNA sequences
(neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Estrogens
Opioids
Prostaglandins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Anti-inflammatory agents
(nonsteroidal; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Drug delivery systems
(oral; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Nerve
(pelvic; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
IT Sexual behavior

(penile erection; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT Ion channel openers
(potassium; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT Anti-inflammatory agents
(steroidal; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT Bombesin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB1, antagonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT Bombesin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB2, antagonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT Bombesin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB3, antagonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT Adrenoceptor antagonists
(.alpha.-; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 72162-96-0, Thromboplastin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-activating factor inhibitors; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-sensitizing agents; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 9036-21-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(III, inhibitors; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 50-56-6, Oxytocin, biological studies 57576-52-0, Thromboxane a2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 138238-81-0, Endothelin converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 9028-35-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors, statins; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 9000-81-1, Acetylcholinesterase 9002-04-4, Thrombin 9025-82-5, Phosphodiesterase 9068-52-4, Phosphodiesterase v 9068-54-6, Phosphodiesterase ii 82785-45-3, Neuropeptide Y
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 9015-82-1, Angiotensin converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(neuropeptide Y inhibitors for treatment of male **sexual**

dysfunction)

IT 58-00-4, Apomorphine 58-18-4, Methyl testosterone 58-22-0, Tostrelle 59-92-7, L Dopa, biological studies 63-05-8D, Androstenedione, derivs. 74-79-3, L Arginine, biological studies 81-81-2, Warfarin 520-85-4, Medroxyprogesterone 521-18-6, Dihydrotestosterone 8001-27-2, Hirudin 9005-49-6, Heparin, biological studies 9039-53-6, Urokinase plasminogen activator 28860-95-9, Carbidopa 29094-61-9, Glipizide 37221-79-7, Vasoactive intestinal peptide 82707-54-8, Neutral endopeptidase 85637-73-6, Atrial natriuretic factor 88150-42-9, Amlodipine 97322-87-7, Rezulin 114471-18-0, Atrial natriuretic peptide b 114798-26-4, Losartan 120014-06-4, Donepezil 127830-04-0, Atrial natriuretic peptide c 128908-32-7, **Melanocortin** 134523-00-5, Atorvastatin 139639-23-9, Tissue plasminogen activator
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transporters for; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)

IT 438443-44-8 438443-45-9 438443-46-0 438443-47-1 438443-48-2
RL: PRP (Properties)
(unclaimed nucleotide sequence; treatment of male **sexual dysfunction**)

IT 438443-49-3
RL: PRP (Properties)
(unclaimed protein sequence; treatment of male **sexual dysfunction**)

IT 438190-17-1
RL: PRP (Properties)
(unclaimed sequence; treatment of male **sexual dysfunction**)

L20 ANSWER 2 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:395983 CA
TITLE: Bombesin receptor antagonists, and combinations with other agents, for the treatment of **sexual dysfunction**
INVENTOR(S): Gonzalez, Maria Isabel; Stock, Herman Thijs; Pinnock, Robert Denham; Pritchard, Martyn Clive; Wayman, Christopher Peter; Van der Graaf, Pieter Hadewijn; Naylor, Alisdair Mark; Higginbottom, Michael
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 225 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040008	A2	20020523	WO 2001-GB5018	20011114

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2002040022 A1 20020523 WO 2000-GB4380 20001117

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2000-GB4380 W 20001117
GB 2001-9910 A 20010423
GB 2001-11037 A 20010504

OTHER SOURCE(S): MARPAT 136:395983

AB Bombesin receptor antagonists have been found to be useful in the treatment of **sexual dysfunction** in both males and females. They may be selective BB1 antagonists or mixed BB1/BB2 antagonists. Combinations are disclosed of bombesin receptor antagonists with a range of other active compds., for example phosphodiesterase V inhibitors, neutral endopeptidase inhibitors, and lasofoxifene. Prepn. of compds. of the invention is described.

TI Bombesin receptor antagonists, and combinations with other agents, for the treatment of **sexual dysfunction**

AB Bombesin receptor antagonists have been found to be useful in the treatment of **sexual dysfunction** in both males and females. They may be selective BB1 antagonists or mixed BB1/BB2 antagonists. Combinations are disclosed of bombesin receptor antagonists with a range of other active compds., for example phosphodiesterase V inhibitors, neutral endopeptidase inhibitors, and lasofoxifene. Prepn. of compds. of the invention is described.

ST bombesin receptor antagonist **sexual dysfunction** treatment; phosphodiesterase inhibitor bombesin antagonist **sexual dysfunction** treatment; neutral endopeptidase inhibitor bombesin antagonist prepn **sexual dysfunction** treatment; lasofoxifene bombesin antagonist **sexual dysfunction** treatment

IT Nervous system agents
(CNS-active; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Oxytocin receptors
Vasopressin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists and modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT VIP receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Estrogens
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and agonists and antagonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Prostaglandins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(and prostaglandin esters; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Gastrin-releasing peptide receptors
Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Steroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Behavior
(arousal, sexual arousal disorders; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 5-HT agonists
5-HT antagonists
Angiotensin receptor antagonists
Anti-inflammatory agents
Anticholesteremic agents
Anticoagulants
Antidiabetic agents
Dopamine agonists
Drug delivery systems
Drug interactions
Hormone replacement therapy
Human
Opioid antagonists
Platelet aggregation inhibitors
Purinoceptor agonists
Vasodilators
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Bombesin receptors
Sex hormones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Opioids
Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Ion channel blockers
(calcium; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Resolution (separation)
(chromatog.; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Sexual behavior
(disorder; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dopamine-transporting, modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual**

dysfunction)
IT Drugs
(drug-induced **sexual dysfunction**; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Alkaloids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ergot; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Drug delivery systems
(implants, testosterone; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Sexual behavior
(impotence; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin**, agonists and modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT 5-HT receptors
Cannabinoid receptors
Estrogen receptors
Opioid receptors
Potassium channel
Purinoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Anti-inflammatory agents
(nonsteroidal; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(norepinephrine-transporting, modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Drug delivery systems
(oral; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Ion channel openers
(potassium; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serotonin-transporting, modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Antidepressants
(**sexual dysfunction** induced by; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Analgesics
(sexual pain disorders; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
IT Bombesin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(type BB1, antagonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Bombesin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB2, antagonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Adrenoceptor antagonists
(.alpha.-; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 57576-52-0, Thromboxane A2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 58-22-0, Testosterone
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and replacement agents; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 50-28-2, Estradiol, biological studies 9002-62-4, Prolactin, biological studies 9002-67-9, Luteinizing hormone 9002-68-0, Follicle-stimulating hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 57-83-0, Progesterone, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 425638-88-6P 425638-90-0P 425638-92-2P 425638-94-4P 425638-96-6P
425638-98-8P 425639-00-5P 425639-02-7P 425639-04-9P 425639-07-2P
425639-10-7P 425639-13-0P 425639-16-3P 425639-19-6P 425639-22-1P
425639-25-4P 425639-28-7P 425639-31-2P 425639-33-4P 425639-35-6P
425639-37-8P 425639-39-0P 425639-41-4P 425639-43-6P 425639-45-8P
425639-47-0P 425639-48-1P 425639-49-2P 425639-50-5P 425639-53-8P
425639-55-0P 425639-57-2P 425639-59-4P 425639-61-8P 425639-65-2P
425639-68-5P 425639-70-9P 425639-72-1P 425639-74-3P 425639-76-5P
425639-77-6P 425639-79-8P 425639-81-2P 425639-83-4P 425639-85-6P
425639-87-8P 425639-89-0P 425639-91-4P 425639-93-6P 425639-95-8P
425639-96-9P 425639-97-0P 425639-98-1P 425639-99-2P 425640-00-2P
425640-01-3P 425640-02-4P 425640-03-5P 425640-15-9P 425640-23-9P
425641-28-7P 429657-44-3P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 50-50-0, Estradiol benzoate 102577-19-5, Neuromedin B
RL: PAC (Pharmacological activity); BIOL (Biological study)
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 426213-31-2P 426213-32-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 58-18-4, Methyl testosterone 59-92-7, biological studies 71-58-9, Medroxyprogesterone acetate 520-85-4, Medroxyprogesterone 521-18-6, Dihydrotestosterone 28860-95-9, Carbidopa 37221-79-7, Vasoactive intestinal polypeptide 37221-79-7D, Vasoactive intestinal polypeptide, analogs 114798-26-4, Losartan 204066-72-8 204066-73-9 204066-75-1 204066-76-2 204066-78-4 204066-79-5 204066-80-8 204066-82-0 204066-83-1 204066-84-2 204066-86-4 204066-87-5 204066-89-7 204066-93-3 204066-95-5 204067-01-6 204067-38-9 215297-27-1 425640-04-6 425640-06-8 425640-08-0 425640-09-1 425640-10-4 425640-11-5 425640-12-6 425640-14-8 425640-17-1 425640-18-2 425640-20-6 425640-21-7 425640-24-0 425640-26-2 425640-28-4 425640-30-8 425640-32-0 425640-34-2 425640-36-4 425640-38-6 425640-39-7 425640-40-0 425640-41-1 425640-43-3 425640-45-5 425640-47-7 425640-49-9 425640-51-3 425640-53-5 425640-55-7 425640-57-9 425640-59-1 425640-60-4 425640-62-6 425640-66-0 425640-68-2 425640-70-6 425640-72-8 425640-74-0 425640-76-2 425640-78-4 425640-80-8 425640-82-0 425640-83-1 425640-84-2 425640-85-3 425640-86-4 425640-87-5 425640-88-6 425640-89-7 425640-90-0 425640-91-1 425640-92-2 425640-93-3 425640-94-4 425640-95-5 425640-96-6 425640-97-7 425640-98-8 425640-99-9 425641-00-5 425641-01-6 425641-02-7 425641-03-8 425641-04-9 425641-05-0 425641-06-1 425641-07-2 425641-08-3 425641-09-4 425641-10-7 425641-11-8 425641-12-9 425641-13-0 425641-14-1 425641-15-2 425641-16-3 425641-17-4 425641-18-5 425641-19-6 425641-20-9 425641-21-0 425641-22-1 425641-23-2 425641-24-3 425641-25-4 425641-26-5 425641-27-6 425641-29-8 425641-30-1 428864-38-4 428864-39-5 428864-40-8 428864-41-9 428864-42-0 428864-43-1 428864-44-2 428864-45-3 428864-46-4 428864-47-5 428864-48-6 428864-49-7 428864-50-0 428864-51-1 428864-52-2 428864-53-3 428864-54-4 428864-55-5 428864-56-6 428864-57-7 428864-58-8 428864-59-9 428864-63-5 428864-64-6 428864-66-8 428864-67-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 388630-36-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 337962-74-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 128908-32-7, **Melanocortin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhancers; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 9000-81-1, Acetylcholinesterase 9025-82-5, Phosphodiesterase 9068-52-4, Phosphodiesterase V 82707-54-8, Neutral endopeptidase 82785-45-3, Neuropeptide Y
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 9088-07-7, Natriuretic factor

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 25506-37-0P 31558-54-0P 63430-65-9P 73717-05-2P 97534-88-8P
97557-59-0P 105754-24-3P 137140-98-8P 158556-65-1P 158951-86-1P
159672-85-2P 159672-86-3P 160233-08-9P 172154-13-1P 172154-15-3P
172154-17-5P 172154-18-6P 204067-15-2P 204067-16-3P 204067-17-4P
291761-10-9P 337962-91-1P 388630-99-7P 425641-31-2P 425641-32-3P
425641-33-4P 425641-34-5P 425641-39-0P 425641-46-9P 425641-47-0P
425641-48-1P 425641-49-2P 425641-50-5P 425641-51-6P 425641-52-7P
425641-53-8P 428864-72-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 55-22-1, Isonicotinic acid, reactions 62-23-7, 4-Nitrobenzoic acid
65-85-0, Benzoic acid, reactions 74-11-3, 4-Chlorobenzoic acid
85-46-1, 1-Naphthalenesulfonyl chloride 86-59-9, Quinoline-8-carboxylic acid 88-13-1, Thiophene-3-carboxylic acid 88-14-2, Furan-2-carboxylic acid 89-95-2 93-03-8 93-11-8, 2-Naphthalenesulfonyl chloride
93-25-4, (2-Methoxyphenyl)acetic acid 98-31-7 98-59-9 98-60-2
98-74-8 98-98-6, Pyridine-2-carboxylic acid 99-04-7, 3-Methylbenzoic acid 99-64-9, 3-Dimethylaminobenzoic acid 99-81-0 99-94-5,
4-Methylbenzoic acid 100-09-4, 4-Methoxybenzoic acid 104-01-8,
(4-Methoxyphenyl)acetic acid 104-03-0, (4-Nitrophenyl)acetic acid
105-13-5 108-86-1, Bromobenzene, reactions 118-90-1, 2-Methylbenzoic acid 118-91-2, 2-Chlorobenzoic acid 121-51-7 122-78-1,
Benzeneacetaldehyde 156-38-7, (4-Hydroxyphenyl)acetic acid 349-75-7
349-88-2 349-95-1 445-29-4, 2-Fluorobenzoic acid 446-51-5
451-82-1, (2-Fluorophenyl)acetic acid 488-93-7, Furan-3-carboxylic acid
527-72-0, Thiophene-2-carboxylic acid 535-80-8, 3-Chlorobenzoic acid
552-16-9, 2-Nitrobenzoic acid 555-16-8, 4-Nitrobenzaldehyde, reactions
579-75-9, 2-Methoxybenzoic acid 586-38-9, 3-Methoxybenzoic acid
587-03-1 589-18-4 591-17-3, 1-Bromo-3-methylbenzene 605-65-2
610-16-2, 2-Dimethylaminobenzoic acid 612-16-8 613-89-8 615-18-9,
2-Chlorobenzoxazole 619-25-0 619-73-8 621-36-3, m-Tolylacetic acid
621-37-4, (3-Hydroxyphenyl)acetic acid 622-47-9, p-Tolylacetic acid
644-36-0, o-Tolylacetic acid 673-06-3, D-Phenylalanine 701-27-9
776-04-5 777-44-6 873-76-7 874-97-5 877-65-6 879-65-2,
Quinoxaline-2-carboxylic acid 931-97-5, 1-Hydroxycyclohexanecarbonitrile
934-60-1, 6-Methylpyridine-2-carboxylic acid 1477-50-5,
1H-Indole-2-carboxylic acid 1592-38-7, 2-Naphthalenemethanol 1656-44-6
1670-81-1, 1H-Indole-5-carboxylic acid 1670-82-2, 1H-Indole-6-carboxylic acid 1670-83-3, 1H-Indole-7-carboxylic acid 1777-82-8 1805-32-9
1877-72-1, 3-Cyanobenzoic acid 1899-93-0 1918-79-2,
5-Methylthiophene-2-carboxylic acid 1939-99-7, Benzenemethanesulfonyl chloride 2104-06-5 2124-55-2, 1H-Indole-4-carboxylic acid 2688-90-6,
[1,1'-Biphenyl]-2-sulfonyl chloride 2766-74-7 2888-06-4 2905-21-7
2905-23-9 2991-42-6 3405-77-4, 5-Methylisoxazole-3-carboxylic acid
3622-35-3, Benzothiazole-6-carboxylic acid 4052-30-6,
4-Methanesulfonylbenzoic acid 4254-29-9 4265-16-1,
Benzofuran-2-carbaldehyde 4533-95-3 4533-96-4 4780-79-4,
1-Naphthalenemethanol 5345-27-7 6314-28-9, Benzo[b]thiophene-2-carboxylic acid 6624-49-3, Isoquinoline-3-carboxylic acid 6964-21-2,
3-Thiopheneacetic acid 6973-60-0 7693-46-1, p-Nitrophenyl chloroformate 10130-74-2 10333-68-3, 2-Pyrrol-1-ylbenzoic acid
13826-35-2 14068-53-2, 2-Amino-5-ethyl-1,3,4-thiadiazole 15084-51-2
16136-58-6, 1-Methyl-1H-indole-2-carboxylic acid 16629-19-9,
2-Thiophenesulfonyl chloride 16709-25-4 17078-28-3,

(4-Dimethylaminophenyl)acetic acid 17849-38-6 18704-37-5, 8-Quinolinesulfonyl chloride 23095-31-0 23806-24-8, 3-Methylthiophene-2-carboxylic acid 23814-12-2, 1H-Benzotriazole-5-carboxylic acid 24424-99-5, Di-tert-butyl dicarbonate 24974-75-2 26638-43-7 28286-86-4 38594-42-2 39774-26-0, 2-Bromo-6-phenylpyridine 42413-03-6 49584-26-1 51527-73-2 54997-92-1 56542-67-7 56946-83-9 59337-92-7 69360-26-5 71648-21-0 73713-79-8 80466-79-1 82964-91-8 88398-93-0 91170-93-3 94108-56-2 99924-18-2 100516-88-9, 6-Quinolinemethanol 114322-14-4, 2,1,3-Benzoxadiazole-4-sulfonyl chloride 118783-85-0 137049-00-4 137049-02-6 142854-50-0 151858-64-9 160233-27-2 166964-37-0 185908-35-4 204067-08-3 204067-12-9 206262-15-9 206262-83-1 216394-05-7 216394-11-5 425641-35-6 425641-36-7 425641-37-8 425641-38-9 425641-40-3 425641-41-4 425641-42-5 425641-43-6 425641-45-8 426213-33-4 426213-34-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sensitizing agents; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 125978-95-2, Nitric oxide synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(substrates; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

L20 ANSWER 3 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:216648 CA
TITLE: Preparation of substituted piperidines as **melanocortin** receptor agonists
INVENTOR(S): Bakshi, Raman K.; Barakat, Khaled J.; Lai, Yingjie; Nargund, Ravi P.; Palucki, Brenda L.; Park, Min K.; Patchett, Arthur A.; Sebhat, Iyassu; Ye, Zhixiong
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015909	A1	20020228	WO 2001-US25757	20010817
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001088285	A5	20020304	AU 2001-88285	20010817

PRIORITY APPLN. INFO.: US 2000-227180P P 20000823
WO 2001-US25757 W 20010817

OTHER SOURCE(S): MARPAT 136:216648
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; X = C1-8 alkyl, alkylenecycloalkyl, alkylenearyl, alkyleneheteroaryl, etc.; X = C1-8 alkyl, alkylenecycloalkyl, alkylenearyl, alkyleneheteroaryl, etc.; R1 = H, C1-8 alkyl, alkylenecycloalkyl, alkylenearyl, alkyleneheteroaryl; Q = amino-tetrahydronaphthyl, amino-benzocycloheptyl, methylamino-tetrahydronaphthyl, aminoindanyl, amino-benzothiopyranyl, amino-1,4-dihydro-1,4-methanonaphthyl, etc.; n = 0, 1, 2], stereoisomers, and pharmaceutically acceptable salts are prepd. as agonists of the human **melanocortin** receptors and, in particular, as selective agonists of the human **melanocortin**-4 receptor (MC-4R). Title compds. I are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. Pharmaceutical compn. including title compds. I and second active ingredient are claimed. Thus, the title compd. II was prepd. from 4-F-D-Phe-4-cyclohexyl-piperidine-4-carboxylic acid Et ester HCl salt and cis-1,2,3,4-tetrahydro-1-tert-butoxycarbonyl-naphthalene-2-carboxylic acid, which was prepd. from 1,2-dihydroaphthalene, ClSO2NCO.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of substituted piperidines as **melanocortin** receptor agonists

AB Title compds. [I; X = C1-8 alkyl, alkylenecycloalkyl, alkylenearyl, alkyleneheteroaryl, etc.; X = C1-8 alkyl, alkylenecycloalkyl, alkylenearyl, alkyleneheteroaryl, etc.; R1 = H, C1-8 alkyl, alkylenecycloalkyl, alkylenearyl, alkyleneheteroaryl; Q = amino-tetrahydronaphthyl, amino-benzocycloheptyl, methylamino-tetrahydronaphthyl, aminoindanyl, amino-benzothiopyranyl, amino-1,4-dihydro-1,4-methanonaphthyl, etc.; n = 0, 1, 2], stereoisomers, and pharmaceutically acceptable salts are prepd. as agonists of the human **melanocortin** receptors and, in particular, as selective agonists of the human **melanocortin**-4 receptor (MC-4R). Title compds. I are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. Pharmaceutical compn. including title compds. I and second active ingredient are claimed. Thus, the title compd. II was prepd. from 4-F-D-Phe-4-cyclohexyl-piperidine-4-carboxylic acid Et ester HCl salt and cis-1,2,3,4-tetrahydro-1-tert-butoxycarbonyl-naphthalene-2-carboxylic acid, which was prepd. from 1,2-dihydroaphthalene, ClSO2NCO.

ST piperidine prepn **melanocortin** receptor agonist

IT Sexual behavior
(disorder; prepn. of substituted piperidines as **melanocortin** receptor agonists)

IT Sexual behavior
(impotence; prepn. of substituted piperidines as **melanocortin** receptor agonists)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** 4; prepn. of substituted piperidines as **melanocortin** receptor agonists)

IT Pituitary hormone receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin**; prepn. of substituted piperidines as **melanocortin** receptor agonists)

IT Diabetes mellitus
Human
Obesity
(prepn. of substituted piperidines as **melanocortin** receptor agonists)

IT 401842-86-2P 401842-90-8P 401842-92-0P 401842-94-2P 401842-95-3P
401842-96-4P 401842-98-6P 401842-99-7P 401843-01-4P 401843-02-5P
401843-03-6P 401843-04-7P 401843-05-8P 401843-06-9P 401843-07-0P
401843-08-1P 401843-09-2P 401843-10-5P 401843-11-6P 401843-12-7P
401843-13-8P 401843-14-9P 401843-15-0P 401843-16-1P 401843-17-2P
401843-18-3P 401843-19-4P 401843-20-7P 401843-21-8P 401843-22-9P
401843-23-0P 401843-24-1P 401843-25-2P 401843-26-3P 401843-28-5P
401843-29-6P 401843-31-0P 401843-32-1P 401843-33-2P 401843-34-3P
401843-35-4P 401843-36-5P 401843-37-6P 401843-38-7P 401843-39-8P
401843-40-1P 401843-41-2P 401843-44-5P 401843-58-1P 401843-59-2P
401843-60-5P 401843-61-6P 401843-62-7P 401843-63-8P 401843-64-9P
401843-65-0P 401843-66-1P 401843-67-2P 401843-68-3P 401843-69-4P
401843-94-5P 401915-20-6P 401915-23-9P 401915-27-3P 401915-31-9P
401915-33-1P 401915-36-4P 401915-38-6P 401915-41-1P 401915-42-2P
401915-43-3P 401915-44-4P 401915-46-6P 401915-47-7P 401915-48-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted piperidines as **melanocortin** receptor agonists)

IT 124-68-5 447-53-0 826-73-3, 1-Benzosuberone 1189-71-5, Chlorosulfonyl isocyanate 2749-11-3, (S)-(+)-2-Amino-1-propanol 4453-90-1, 1,4-Dihydro-1,4-methanonaphthalene 10316-79-7, 1-Aminocyclopentanemethanol 22059-21-8, 1-Aminocyclopropane-1-carboxylic acid 29059-07-2, Tetralone 57292-44-1 57292-45-2 312638-87-2 401843-95-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of substituted piperidines as **melanocortin** receptor agonists)

IT 95-13-6P, Indene 4373-13-1P 7125-62-4P 14944-28-6P 35550-94-8P 40073-45-8P 59433-90-8P 132565-21-0P 363192-22-7P 363192-23-8P 363192-24-9P 363192-25-0P 363192-26-1P 363192-27-2P 363192-28-3P 363192-29-4P 363192-30-7P 363192-31-8P 363192-32-9P 363192-33-0P 363192-34-1P 363192-35-2P 378741-77-6P 378741-78-7P 401843-45-6P 401843-46-7P 401843-47-8P 401843-48-9P 401843-49-0P 401843-50-3P 401843-51-4P 401843-52-5P 401843-53-6P 401843-55-8P 401843-56-9P 401843-57-0P 401843-70-7P 401843-73-0P 401843-74-1P 401843-75-2P 401843-76-3P 401843-77-4P 401843-78-5P 401843-79-6P 401843-80-9P 401843-81-0P 401843-82-1P 401843-88-7P 401843-90-1P 401843-91-2P 401843-92-3P 401843-93-4P 401843-96-7P 401843-97-8P 401843-98-9P 401843-99-0P 401915-50-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of substituted piperidines as **melanocortin** receptor agonists)

L20 ANSWER 4 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:167180 CA
TITLE: Preparation of N-(benzylideneamino)guanidines and N-(benzylideneamino)-N'-hydroxyguanidines and their use as **melanocortin** receptor ligands
INVENTOR(S): Lundstedt, Torbjoern; Skottner, Anna; Seifert,

Elisabeth
PATENT ASSIGNEE(S): Melacure Therapeutics AB, Swed.
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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PRIORITY APPLN. INFO.: GB 2000-19357 A 20000807
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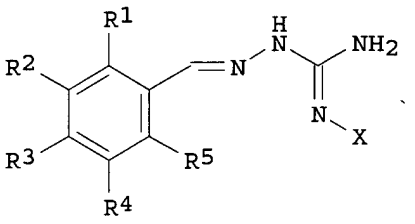

I

AB The present invention relates to the use of compds. of general formula (I; wherein X is H or OH; R1 - R5 are the same or different and are selected from hydrogen, halogen, alkyl having 1 to 5 carbon atoms, electron donor groups such as alkoxy having 1-5 carbon atoms or hydroxy, electron acceptor groups (selected from cyano, nitro, trifluoroalkyl or amide), alkylamino, benzoyloxy, nitroxy, Ph or sulfo) and the pharmacol. active salts thereof as ligands to the **melanocortin** receptors and/or for treatment of disorders in the **melanocortin** system. The above disorders related to the **melanocortin** system are inflammation, mental disorders, sexual functions and/**sexual dysfunctions**, drug-induced or other disorders of the blood and/or lymphoid system, allergic disorders, disorders of cardiovascular system, pain, diabetes type II, obesity, anorexic conditions (those caused by cancer, cachexia, geriatric conditions, HIV, trauma, and psychol. conditions), peripheral nerve regeneration, central nerve regeneration, skin disorders including melanoma, or ischemia and/or ischemia/reperfusion. These compds. are also useful for the treatment of dysfunctions of the endocrine system or an hormonal system, inducing skin tanning or for inducing lighter skin color, and for the treatment and/or diagnosis of malignancies such as melanoma and metastasis. A soln. of

2-chloro-3,4-dimethoxybenzaldehyde (1.0 g, 5 mmol), aminoguanidine bicarbonate (0.68 g, 5 mmol) and acetic acid (1 mL) in 15 mL of methanol was heated at reflux for 10 min to give 70% N-(2-chloro-3,4-dimethoxybenzylideneamino)guanidine acetate. N-(5-Chloro-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate in vitro showed the binding affinity to MC1, MC3, MC4, and MC5 receptor with Ki of 6.4, 1, 17.1, and 8.7 .mu.M, resp.

TI Preparation of N-(benzylideneamino)guanidines and N-(benzylideneamino)-N'-hydroxyguanidines and their use as **melanocortin** receptor ligands

AB The present invention relates to the use of compds. of general formula (I; wherein X is H or OH; R1 - R5 are the same or different and are selected from hydrogen, halogen, alkyl having 1 to 5 carbon atoms, electron donor groups such as alkoxy having 1-5 carbon atoms or hydroxy, electron acceptor groups (selected from cyano, nitro, trifluoroalkyl or amide), alkylamino, benzoyloxy, nitroxy, Ph or sulfo) and the pharmacol. active salts thereof as ligands to the **melanocortin** receptors and/or for treatment of disorders in the **melanocortin** system. The above disorders related to the **melanocortin** system are inflammation, mental disorders, sexual functions and/**sexual dysfunctions**, drug-induced or other disorders of the blood and/or lymphoid system, allergic disorders, disorders of cardiovascular system, pain, diabetes type II, obesity, anorexic conditions (those caused by cancer, cachexia, geriatric conditions, HIV, trauma, and psychol. conditions), peripheral nerve regeneration, central nerve regeneration, skin disorders including melanoma, or ischemia and/or ischemia/reperfusion. These compds. are also useful for the treatment of dysfunctions of the endocrine system or an hormonal system, inducing skin tanning or for inducing lighter skin color, and for the treatment and/or diagnosis of malignancies such as melanoma and metastasis. A soln. of 2-chloro-3,4-dimethoxybenzaldehyde (1.0 g, 5 mmol), aminoguanidine bicarbonate (0.68 g, 5 mmol) and acetic acid (1 mL) in 15 mL of methanol was heated at reflux for 10 min to give 70% N-(2-chloro-3,4-dimethoxybenzylideneamino)guanidine acetate. N-(5-Chloro-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate in vitro showed the binding affinity to MC1, MC3, MC4, and MC5 receptor with Ki of 6.4, 1, 17.1, and 8.7 .mu.M, resp.

ST benzylideneaminoguanidine benzylideneaminohydroxyguanidine prepn **melanocortin** receptor ligand; disorder **melanocortin** system benzylideneaminohydroxyguanidine prepn; inflammation benzylideneaminohydroxyguanidine prepn; mental disorder benzylideneaminohydroxyguanidine prepn; sexual function benzylideneaminohydroxyguanidine prepn; allergy treatment benzylideneaminohydroxyguanidine prepn; cardiovascular system disorder treatment benzylideneaminohydroxyguanidine prepn; pain diabetes type II treatment benzylideneaminohydroxyguanidine prepn; obesity treatment benzylideneaminohydroxyguanidine prepn; anorexia treatment benzylideneaminohydroxyguanidine prepn

IT Diagnosis
(agents, for melanoma or cancer metastasis; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Melanoma
(anticancer and diagnostic agents for; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Nervous system
(central, degeneration; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for

treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Neoplasm
(diagnostic agents for; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Blood
Endocrine system
Lymph node
(disease; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Sexual behavior
(disorder; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Hormones, animal, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(disorders; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin**; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Antitumor agents
(melanoma; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Neoplasm
(metastasis, diagnostic agents for; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Regeneration, animal
(nerve, peripheral; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Diabetes mellitus
(non-insulin-dependent; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Allergy inhibitors
Analgesics
Anorexia
Anti-inflammatory agents
Antiobesity agents
Cardiovascular agents
Ischemia
Mental disorder
Reperfusion

Skin, disease
(prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Cosmetics
(skin-lightening; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Skin
(tanning inducers; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT 128908-32-7P, **Melanocortin**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT 25054-35-7P, N-(2,4-Dinitrobenzylideneamino)guanidine acetate 65565-57-3P, N-(Benzylideneamino)guanidine acetate 85894-20-8P, N-(3-Iodobenzylideneamino)-N'-hydroxyguanidine tosylate 87861-89-0P, N-(3-Methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 96826-46-9P, N-(3-Nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 96826-48-1P, N-(4-Cyanobenzylideneamino)-N'-hydroxyguanidine tosylate 96826-50-5P, N-(4-Chloro-3-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 96826-65-2P, N-(2,5-Dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 123541-21-9P, N-(2,3,4-Trihydroxybenzylideneamino)-N'-hydroxyguanidine tosylate 123541-25-3P, N-(2-Hydroxybenzylideneamino)-N'-hydroxyguanidine tosylate 131610-93-0P, N-(2,4-Dihydroxybenzylideneamino)-N'-hydroxyguanidine tosylate 131610-95-2P, N-(2-Hydroxy-4-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 131610-97-4P, N-(2-Hydroxy-4,6-dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 131610-99-6P, N-(2-Hydroxy-5-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 131611-00-2P, N-(Benzylideneamino)-N'-hydroxyguanidine tosylate 139613-32-4P, N-(3-Fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 139613-44-8P, N-(3-Hydroxy-4-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 148796-78-5P, N-(5-Bromo-2-hydroxybenzylideneamino)-N'-hydroxyguanidine tosylate 160486-31-7P, N-(4-Dimethylaminobenzylideneamino)-N'-hydroxyguanidine tosylate 160916-41-6P, N-(4-Methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 161016-41-7P, N-(3,4-Methylenedioxybenzylideneamino)-N'-hydroxyguanidine tosylate 161016-43-9P, N-(2,3,4-Trimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 161016-44-0P, N-(2,4,5-Trimethoxybenzylideneamino)-N'-hydroxyguanidine 161016-45-1P, N-(2,4,5-Trimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 161016-47-3P, N-(2,4,6-Trimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 161016-49-5P, N-(3,4,5-Trimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 170996-62-0P, N-(3-Bromo-4-methoxybenzylideneamino)guanidine hydrochloride 208582-89-2P, N-(3,4-Dimethoxy-2-chlorobenzylideneamino)-N'-hydroxyguanidine tosylate 208583-03-3P, N-(3-Bromo-4-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 219924-72-8P, N-(2-Sulfobenzylideneamino)-N'-hydroxyguanidine 284042-43-9P, N-(3,4-Dimethoxy-2-chlorobenzylideneamino)guanidine 332395-03-6P 332395-39-8P, N-(2-Chloro-3,4-dimethoxybenzylideneamino)guanidine acetate

332395-47-8P, N-(3,4,5-Trimethoxybenzylideneamino)guanidine acetate
332395-48-9P, N-(2,4,6-Trimethoxybenzylideneamino)guanidine acetate
332395-49-0P, N-(3-Nitrobenzylideneamino)guanidine acetate 332395-50-3P,
N-(2-Hydroxy-4,6-dimethoxybenzylideneamino)guanidine acetate
332395-51-4P, N-(4-Nitrobenzylideneamino)guanidine acetate 332395-52-5P,
N-(3-Bromo-4-fluorobenzylideneamino)guanidine acetate 332395-53-6P,
N-(2,3-Difluorobenzylideneamino)guanidine acetate 332395-54-7P,
N-(4-Chloro-3-fluorobenzylideneamino)guanidine acetate 332395-55-8P,
N-(3-Methoxy-2,6-dinitrobenzylideneamino)guanidine hydrochloride
332395-56-9P, N-(3-Bromo-2,6-dinitrobenzylideneamino)guanidine
hydrochloride 332395-57-0P, N-(2,3-Dimethoxy-5,6-
dinitrobenzylideneamino)guanidine acetate 332395-58-1P,
N-(5-Bromo-2,4-dimethoxybenzylideneamino)guanidine acetate 332395-59-2P,
N-(2,3-Dimethoxy-5-nitrobenzylideneamino)guanidine acetate 332395-60-5P,
N-(4-Phenylbenzylideneamino)guanidine acetate 332395-61-6P,
N-(3,4-Difluorobenzylideneamino)guanidine acetate 332395-62-7P,
N-(2-Fluoro-5-nitrobenzylideneamino)guanidine acetate 332395-63-8P,
N-(4-Bromo-2-fluorobenzylideneamino)guanidine acetate 332395-64-9P,
N-(3,5-Dichlorobenzylideneamino)guanidine acetate 332395-65-0P,
N-(3,5-Dinitrobenzylideneamino)guanidine acetate 332395-66-1P,
N-(2,6-Difluorobenzylideneamino)guanidine acetate 332395-67-2P,
N-(3-Chloro-4-fluorobenzylideneamino)guanidine acetate 332395-68-3P,
N-(2-Bromo-4-nitrobenzylideneamino)guanidine acetate 332395-69-4P,
N-(2-Bromo-5-nitrobenzylideneamino)guanidine acetate 332395-70-7P,
N-(2-Iodobenzylideneamino)guanidine acetate 332395-71-8P,
N-(2,3-Dimethoxy-5-nitrobenzylideneamino)guanidine hydrochloride
332395-72-9P, N-(2-Hydroxy-4-methoxybenzylideneamino)guanidine acetate
332395-73-0P, N-(4-Bromo-3-nitrobenzylideneamino)guanidine acetate
332395-74-1P, N-(6-Chloro-2,3-dinitrobenzylideneamino)guanidine
hydrochloride 332395-75-2P, N-(3-Iodobenzylideneamino)guanidine
hydrochloride 332395-76-3P, N-(2-Sulfobenzylideneamino)guanidine
hydrochloride 332395-77-4P, N-(3,4-Dichlorobenzylideneamino)guanidine
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acetate 332395-79-6P, N-(4-Chloro-3-nitrobenzylideneamino)guanidine
acetate 332395-80-9P, N-(4-Fluoro-3-nitrobenzylideneamino)guanidine
acetate 332395-81-0P, N-(4-Methoxy-3-nitrobenzylideneamino)guanidine
acetate 332395-83-2P, N-(3,5-Dichloro-2-nitrobenzylideneamino)guanidine
acetate 332395-84-3P, N-(2-Hydroxy-3-methoxy-5-
nitrobenzylideneamino)guanidine hydrochloride 332395-85-4P,
N-(2-Hydroxy-4-methoxy-5-nitrobenzylideneamino)guanidine hemiacetate
332395-86-5P, N-(3-Chloro-4-methoxy-5-nitrobenzylideneamino)guanidine
acetate 332395-87-6P, N-(3,5-Dichloro-4-methoxybenzylideneamino)guanidin
e acetate 332395-88-7P, N-(3-Bromo-4-methoxy-5-
methylbenzylideneamino)guanidine acetate 332395-89-8P,
N-(2,3,4-Trimethoxybenzylideneamino)guanidine hydrochloride
332395-90-1P, N-(4-Chloro-2-methoxy-5-nitrobenzylideneamino)guanidine
acetate 332395-91-2P, N-(3,6-Dichloro-2-nitrobenzylideneamino)guanidine
acetate 332395-92-3P, N-(2-Hydroxy-4-methyl-5-
nitrobenzylideneamino)guanidine hydrochloride 332395-93-4P,
N-(2-Bromo-5-chloro-3-nitrobenzylideneamino)guanidine acetate
332395-94-5P, N-(3-Hydroxy-4-methyl-2-nitrobenzylideneamino)guanidine
acetate 332395-95-6P, N-(5-Bromo-4-methyl-2-
nitrobenzylideneamino)guanidine hydrochloride 332395-96-7P,
N-(5-Bromo-2-hydroxy-3-nitrobenzylideneamino)guanidine hydrochloride
332395-97-8P, N-(5-Bromo-2-methoxy-3-nitrobenzylideneamino)guanidine
hydrochloride 332395-98-9P, N-(2,4-Dimethoxy-5-
nitrobenzylideneamino)guanidine acetate 332395-99-0P,
N-(4-Bromo-2-fluoro-5-nitrobenzylideneamino)guanidine acetate
398134-07-1P, N-(3-Bromobenzylideneamino)-N'-hydroxyguanidine tosylate
398134-09-3P, N-(5-Chloro-2-nitrobenzylideneamino)-N'-hydroxyguanidine

tosylate 398134-12-8P, N-(2,3-Dihydroxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-14-0P, N-(4,5-Methylenedioxy-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-16-2P, N-(2-Bromobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-18-4P, N-(2,3-Dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-20-8P, N-(2,5-Difluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-22-0P, N-(4-Nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-24-2P, N-(2-Hydroxy-3-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-26-4P, N-(3-Chlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-28-6P, N-(2,3,4-Tribenzyloxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-30-0P, N-(4-Chlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-31-1P, N-(4-Bromobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-33-3P, N-(4-Diethylaminobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-35-5P, N-(4-Hydroxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-37-7P, N-(2-Nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-39-9P, N-(2-Bromo-3,4,5-trimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-41-3P, N-(2,4-Dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-43-5P, N-(2-Chloro-6-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-45-7P, N-(3,5-Dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-47-9P, N-(5-Hydroxy-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-49-1P, N-(3,6-Dimethoxy-2-nitroxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-51-5P, N-(2,3-Dimethoxy-5-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-53-7P, N-(2,3-Dimethoxy-5,6-dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-55-9P, N-(2,6-Dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-57-1P, N-(2,3-Dimethoxy-6-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-58-2P, N-(5-Bromo-2,4-dimethoxybenzylideneamino)-N'-hydroxyguanidine 398134-59-3P, N-(5-Bromo-2,4-dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-61-7P, N-(2-Fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-63-9P, N-(2-Methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-65-1P, N-(2,3-Methylenedioxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-67-3P, N-(4-Bromo-3-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-69-5P, N-(5-Bromo-2-hydroxy-3-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-71-9P, N-(2,3-Dinitro-6-chlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-73-1P, N-(3,6-Dichloro-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-75-3P, N-(2,6-Dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-77-5P, N-(2-Chloro-3,4-dimethoxy-6-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-79-7P, N-(2-Chlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-81-1P, N-(4-Fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-83-3P, N-(4-Fluoro-3-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-85-5P, N-(2-Chloro-5-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-87-7P, N-(4-Chloro-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-89-9P, N-(3,4-Dichlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-91-3P, N-(2,4-Dichlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-93-5P, N-(4-Methoxy-3-nitrobenzylideneamino)-N'-hydroxyguanidine 398134-95-7P, N-(2,3-Dichlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-97-9P, N-(2-Fluoro-5-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-99-1P, N-(2-Methoxy-5-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-01-8P, N-(4-Hydroxy-3,5-dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398135-03-0P, N-(2-Bromo-5-chloro-3-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-05-2P, N-(3-Bromo-2,6-dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-07-4P, N-(3,5-Dinitro-2-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398135-09-6P, N-(5-Bromo-2-hydroxy-3-

nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-11-0P, N-(3-Methoxy-2,6-dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-13-2P, N-(3-Bromo-4-fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-15-4P, N-(2,3-Difluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-17-6P, N-(4-Chloro-3-fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-19-8P, N-(4-Bromo-3-fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-21-2P, N-(3,4-Difluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-23-4P, N-(4-Phenylbenzylideneamino)-N'-hydroxyguanidine tosylate 398135-25-6P, N-(3-Chloro-2,6-dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-27-8P, N-(4-Bromo-2-fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-29-0P, N-(2-Bromo-5-nitrobenzylidenzeamino)-N'-hydroxyguanidine tosylate 398135-30-3P, N-(2,4-Dinitrobenzylideneamino)-N'-hydroxyguanidine hydrochloride 398135-32-5P, N-(2,6-Difluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-34-7P, N-(3-Chloro-4-fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-36-9P, N-(3,5-Dichlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-38-1P, N-(2-Bromo-4-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-40-5P, N-(3,5-Dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-42-7P, N-(2,3-Dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-44-9P, N-(2-Iodobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-46-1P, N-(2-Chloro-3,4,5-trimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398135-48-3P, N-(3,5-Difluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-50-7P, N-(5-Bromo-2,3,4-trimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398135-52-9P, N-(3-Chloro-4-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398135-53-0P, N-(2,3-Dimethoxy-5-nitrobenzylideneamino)-N'-hydroxyguanidine hydrochloride 398135-55-2P, N-(3,5-Difluoro-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-57-4P, N-(3,5-Dichloro-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-58-5P, N-(3,5-Difluoro-2-nitrobenzylideneamino)guanidine acetate 398135-59-6P 398135-60-9P 398135-61-0P 398135-62-1P 398135-63-2P 398135-64-3P 398135-65-4P 398135-66-5P 398135-67-6P 398135-68-7P 398135-69-8P 398135-70-1P 398135-71-2P 398135-72-3P 398135-73-4P 398135-74-5P 398135-75-6P 398135-76-7P 398135-77-8P 398135-78-9P 398135-79-0P 398135-81-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT 2582-30-1, Aminoguanidine bicarbonate 5417-17-4, 2-Chloro-3,4-dimethoxybenzaldehyde

RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

L20 ANSWER 5 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:96099 CA
TITLE: Treatment of male **sexual dysfunction**
INVENTOR(S): Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn; Wayman, Christopher Peter
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 124 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003995	A2	20020117	WO 2001-IB1187	20010702
WO 2002003995	A3	20020418		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002052370	A1	20020502	US 2001-893585	20010628

PRIORITY APPLN. INFO.:

GB 2000-16684	A	20000706
GB 2000-30647	A	20001215
GB 2001-6167	A	20010313
GB 2001-8483	A	20010404
US 2000-219100P	P	20000718
GB 2001-1584	A	20010122
US 2001-274957P	P	20010312

OTHER SOURCE(S): MARPAT 136:96099

AB The present invention relates to the use of neutral endopeptidase inhibitors (NEPi) and a combination of NEPi and phosphodiesterase type (PDE5) inhibitor for the treatment of male **sexual dysfunction**, in particular MED.

TI Treatment of male **sexual dysfunction**

AB The present invention relates to the use of neutral endopeptidase inhibitors (NEPi) and a combination of NEPi and phosphodiesterase type (PDE5) inhibitor for the treatment of male **sexual dysfunction**, in particular MED.

ST male **sexual dysfunction** neutral endopeptidase inhibitor

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ORL1, modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Neuropeptide Y receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Y5, antagonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Neuropeptide Y receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Y1, antagonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT VIP receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (agonists; treatment of male **sexual dysfunction**

using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Endothelin receptors
Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antiestrogens; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Ion channel blockers
(calcium; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Sexual behavior
(disorder, male; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dopamine-transporting, modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Sexual behavior
(ejaculation, disorder; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Alkaloids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ergot; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Anticholesteremic agents
(fibrates and statins; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Sexual behavior
(impotence; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin**, agonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Cannabinoid receptors
Estrogen receptors
Opioid receptors
Oxytocin receptors
Vasopressin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(norepinephrine-transporting, modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Drug delivery systems
(oral; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Ion channel openers
(potassium; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Sexual behavior
(premature ejaculation; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serotonin-transporting, modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Drug delivery systems
(tablets; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 5-HT agonists
5-HT antagonists
Angiotensin receptor antagonists
Anticoagulants
Dopamine agonists
Drug interactions
Drug screening
Opioid antagonists
Platelet aggregation inhibitors
Purinoceptor agonists
Vasodilators
(treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Estrogens
Opioids

Prostaglandins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Adrenoceptor antagonists
(.alpha.-; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 57576-52-0, Thromboxane A2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 82785-45-3, Neuropeptide Y
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors and agonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 128908-32-7, **Melanocortin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhancers; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9028-35-7, HMG-CoA reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, statins; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9000-81-1, Acetylcholinesterase 9040-59-9, Phosphodiesterase II 9068-52-4, Phosphodiesterase V 82707-54-8, Neutral endopeptidase 138238-81-0, Endothelin converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9036-21-9, Phosphodiesterase 8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(isoforms, inhibitors; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9088-07-7, Natriuretic factor 85637-73-6, Atrial natriuretic factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with

phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sensitizing agents; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 125978-95-2, Nitric oxide synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(substrates; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9015-82-1, Angiotensin converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 337962-68-2P 337962-69-3P 337962-70-6P 337962-71-7P 337962-72-8P
337962-73-9P 337962-74-0P 388630-36-2P 388630-55-5P
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 58-22-0, Testosterone 71-58-9, Medroxyprogesterone acetate 520-85-4, Medroxyprogesterone 521-18-6, Dihydrotestosterone 37221-79-7, Vasoactive intestinal peptide 37221-79-7D, Vasoactive intestinal peptide, analogs 139755-83-2, Sildenafil 147676-53-7 171596-29-5, IC-351 215297-27-1 224785-90-4, Vardenafil 334826-98-1 334827-47-3 334827-59-7 335077-64-0 335077-70-8 389128-36-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 98-10-2, Benzenesulfonamide 108-33-8, 2-Amino-5-methyl-1,3,4-thiadiazole 7663-77-6, N-(3-Aminopropyl)-2-pyrrolidinone 14068-53-2, 2-Amino-5-ethyl-1,3,4-thiadiazole 59892-44-3 118755-30-9 118755-86-5 118756-03-9 118783-85-0 118786-35-9 136834-71-4 136834-85-0 136850-24-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

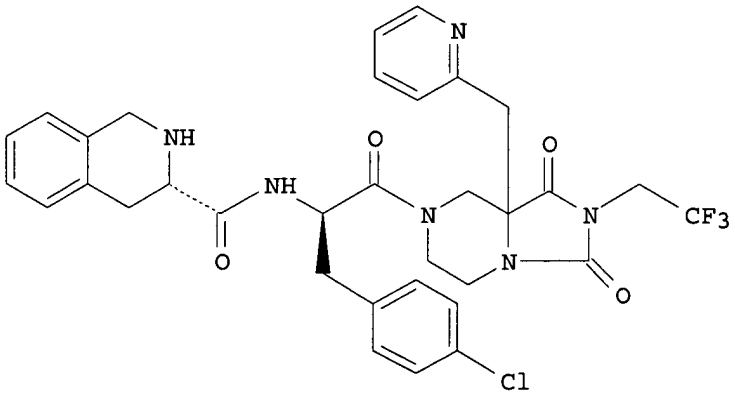
IT 337962-78-4P 337962-79-5P 337962-80-8P 337962-81-9P 337962-83-1P
337962-84-2P 337962-91-1P 337962-93-3P 388630-52-2P 388630-83-9P
388631-26-3P 388631-29-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 388630-37-3P 388630-54-4P 389083-04-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

L20 ANSWER 6 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:69824 CA
TITLE: Preparation of heterocycle compounds as **melanocortin** receptor ligands
INVENTOR(S): Carpino, Philip Albert; Cole, Bridget McCarthy; Morgan, Bradley Paul
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000654	A1	20020103	WO 2001-IB995	20010531
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001060548	A5	20020108	AU 2001-60548	20010531
US 2002072604	A1	20020613	US 2001-891026	20010625

PRIORITY APPLN. INFO.: US 2000-214616P P 20000628
WO 2001-IB995 W 20010531
OTHER SOURCE(S): MARPAT 136:69824
GI



II

AB Compds. represented by formula HET-COCR3R4-NX4-CO(CR6R7)m-D [I; wherein m = 0, 1 or 2; HET = heterocyclyl; R3, R4 = H,, C1-8 alkyl, CH(R8)-aryl, -CH(R8)-heteroaryl, -C0-3 alkyl-C3-8 cycloalkyl (wherein the aryl or heteroaryl groups are optionally substituted by one or two groups; R8 = H, C1-8 alkyl, -C0-3 alkylaryl, -C0-3 alkylheteroaryl, -C3-6 cycloalkyl); R6, R7 = H, C1-6 alkyl, -C0-3 alkyl-aryl, -C0-3 alkyl-heteroaryl, -C0-3 alkyl-C3-8 cycloalkyl; or R6 and R7 together with the nitrogen atom to which they are attached form a 5- or 6-membered ring optionally contg. an addnl. heteroatom selected from O, S, NR3; D = -C0-6 alkylamino-C(:NR7)-NR15R16, -C0-6 alkylaminopyridyl, -C0-6 alkylaminoimidazolyl, -C0-6 alkylaminothiazolyl, -C0-6 alkylaminopyrimidinyl, -C0-6 alkylaminopiperazinyl-R15, -C0-6 alkylmorpholinyl, etc. (wherein R15, R16 = H, -C1-6 alkyl, -C0-3 alkylaryl, -C0-3 alkylheteroaryl, or -C0-3 alkyl-C3-8 cycloalkyl, wherein the alkyl and aryl groups are optionally substituted with one or two groups); X4 = H or C1-6 alkyl or X4 is taken together with R4 and the nitrogen atom to which X4 is attached and the carbon atom to which R4 is attached and form a five to seven membered ring] are prepd. Melanocortins are peptides derived from pro-opiomelanocortins (POMC) that bind to and activate G-protein coupled receptors (GPCR's) of the **melanocortin** receptor family and regulate a diverse no. of physiol. processes including food intake., metab., and thermogenesis as well as **sexual dysfunction**. These compds. I are useful for the treatment or prevention of disorders, diseases, or conditions responsive to the activation of **melanocortin** receptor including obesity, diabetes mellitus, male or female **sexual dysfunction**, erectile dysfunction, or disorders that cause redn. in appetite, or feeding behavior and/or body wt.; for modulating appetite and metabolic rates; for acutely stimulating the appetite for the treatment of hepatic lipidosis, cachexia, and other pathologies resulting in/from inappropriate food intake and wt. loss; for acutely stimulating the appetite of livestock for the treatment of ketosis, postpartum anestrus, and other metabolic and reproductive pathologies resulting in/from inappropriate food intake and wt. loss; and for enhancing growth and survivability of neonates in livestock. Thus, esterification of N-Boc-L-Tic-OH with N-hydroxysuccinimide using Et3N and EDC in CH2Cl2 at room temp. for 4 h gave 3,4-Dihydro-1H-isoquinoline-2,3-(S)-dicarboxylic acid 2-tert-Bu ester 3-(2,5-dioxopyrrolidin-1-yl) ester which was condensed with D-p-chlorophenylalanine in the presence of Et3N in CH2Cl2 at room temp. overnight to give 3-(S)-[(R)-1-Carboxy-2-(4-chlorophenyl)ethylcarbamoyl]-3,4-dihydro-1H-isoquinoline-2-carboxylic acid tert-Bu ester. The latter compd. was further condensed with 8a-(Pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)tetrahydroimidazo[1,5-a]pyrazine-1,3-dione using Et3N and EDC in CH2Cl2 at 0.degree. for 5 h to give (S)-3-[(R)-1-(4-Chlorobenzyl)-2-[1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazin-7-yl]-2-oxoethylcarbamoyl]-3,4-dihydro-1H-isoquinoline-2-carboxylic acid tert-Bu ester which was treated with a mixt. of EtOH and concd. HCl at 0.degree. for 0.5 h to give (S)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid N-[(R)-1-(4-chlorobenzyl)-2-[1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazin-7-yl]-2-oxoethyl]amide (II) hydrochloride which may be considered as a dipeptide analog hepterocycle amide, N-[N-(L-1,2,3,4-Tetrahydroisoquinoline-3-carbonyl)-D-p-chlorophenylalanyl]-1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazine.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of heterocycle compounds as **melanocortin** receptor ligands

AB Compds. represented by formula HET-COCR3R4-NX4-CO(CR6R7)m-D [I; wherein m = 0, 1 or 2; HET = heterocyclyl; R3, R4 = H,, C1-8 alkyl, CH(R8)-aryl,

-CH(R8)-heteroaryl, -C0-3 alkyl-C3-8 cycloalkyl (wherein the aryl or heteroaryl groups are optionally substituted by one or two groups; R8 = H, C1-8 alkyl, -C0-3 alkylaryl, -C0-3 alkylheteroaryl, -C3-6 cycloalkyl); R6, R7 = H, C1-6 alkyl, -C0-3 alkyl-aryl, -C0-3 alkyl-heteroaryl, -C0-3 alkyl-C3-8 cycloalkyl; or R6 and R7 together with the nitrogen atom to which they are attached form a 5- or 6-membered ring optionally contg. an addnl. heteroatom selected from O, S, NR3; D = -C0-6 alkylamino-C(:NR7)-NR15R16, -C0-6 alkylaminopyridyl, -C0-6 alkylaminoimidazolyl, -C0-6 alkylaminothiazolyl, -C0-6 alkylaminopyrimidinyl, -C0-6 alkylaminopiperazinyl-R15, -C0-6 alkylmorpholinyl, etc. (wherein R15, R16 = H, -C1-6 alkyl, -C0-3 alkylaryl, -C0-3 alkylheteroaryl, or -C0-3 alkyl-C3-8 cycloalkyl, wherein the alkyl and aryl groups are optionally substituted with one or two groups); X4 = H or C1-6 alkyl or X4 is taken together with R4 and the nitrogen atom to which X4 is attached and the carbon atom to which R4 is attached and form a five to seven membered ring] are prepd. Melanocortins are peptides derived from pro-opiomelanocortins (POMC) that bind to and activate G-protein coupled receptors (GPCR's) of the **melanocortin** receptor family and regulate a diverse no. of physiol. processes including food intake., metab., and thermogenesis as well as **sexual dysfunction**. These compds. I are useful for the treatment or prevention of disorders, diseases, or conditions responsive to the activation of **melanocortin** receptor including obesity, diabetes mellitus, male or female **sexual dysfunction**, erectile dysfunction, or disorders that cause redn. in appetite, or feeding behavior and/or body wt.; for modulating appetite and metabolic rates; for acutely stimulating the appetite for the treatment of hepatic lipidosis, cachexia, and other pathologies resulting in/from inappropriate food intake and wt. loss; for acutely stimulating the appetite of livestock for the treatment of ketosis, postpartum anestrus, and other metabolic and reproductive pathologies resulting in/from inappropriate food intake and wt. loss; and for enhancing growth and survivability of neonates in livestock. Thus, esterification of N-Boc-L-Tic-OH with N-hydroxysuccinimide using Et3N and EDC in CH2Cl2 at room temp. for 4 h gave 3,4-Dihydro-1H-isoquinoline-2,3-(S)-dicarboxylic acid 2-tert-Bu ester 3-(2,5-dioxopyrrolidin-1-yl) ester which was condensed with D-p-chlorophenylalanine in the presence of Et3N in CH2Cl2 at room temp. overnight to give 3-(S)-[(R)-1-Carboxy-2-(4-chlorophenyl)ethylcarbamoyl]-3,4-dihydro-1H-isoquinoline-2-carboxylic acid tert-Bu ester. The latter compd. was further condensed with 8a-(Pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)tetrahydroimidazo[1,5-a]pyrazine-1,3-dione using Et3N and EDC in CH2Cl2 at 0.degree. for 5 h to give (S)-3-[(R)-1-(4-Chlorobenzyl)-2-[1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazin-7-yl]-2-oxoethylcarbamoyl]-3,4-dihydro-1H-isoquinoline-2-carboxylic acid tert-Bu ester which was treated with a mixt. of EtOH and concd. HCl at 0.degree. for 0.5 h to give (S)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid N-[(R)-1-(4-chlorobenzyl)-2-[1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazin-7-yl]-2-oxoethyl]amide (II) hydrochloride which may be considered as a dipeptide analog hepterocycle amide, N-[N-(L-1,2,3,4-Tetrahydroisoquinoline-3-carbonyl)-D-p-chlorophenylalanyl]-1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazine.

ST heterocyclic compd prepn prevention treatment obesity; **melanocortin** receptor ligand tetrahydroisoquinolinecarboxamide prepn; imidazopyrazine prepn prevention treatment diabetes mellitus **sexual dysfunction**; appetite metabolic rate modulator heterocyclic compd prepn; tetrahydroisoquinolinecarbonylchlorophenylalanine prepn dipeptide analog heterocycle amide

IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amides, dipeptide analog heterocycle amides; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Sexual behavior
(disorder; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Sexual behavior
(impotence; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Ketone bodies
(ketosis, livestock, appetite stimulants in treatment of; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Lipids, processes
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(lipidosis, livestock, appetite stimulants in treatment of; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Newborn
(livestock, enhancers for growth and survivability; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Body weight
(loss; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Pituitary hormone receptors
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(**melanocortin**; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Appetite
Metabolism, animal
(modulators; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Antidiabetic agents
Antiobesity agents
Cachexia
(prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Heterocyclic compounds
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT 252008-71-2P 252008-73-4P 384345-09-9P 384345-10-2P 384345-12-4P 384345-13-5P 384345-15-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

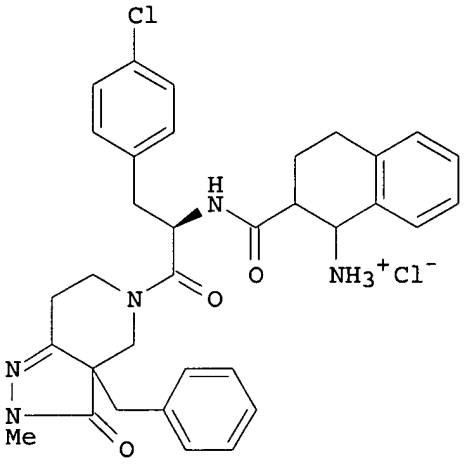
IT 384345-08-8P 384345-11-3P 384345-14-6P 384345-16-8P 384345-17-9P 384345-21-5P 384345-22-6P 384345-23-7P 384345-24-8P 384345-25-9P 384345-26-0P 384345-27-1P 384345-28-2P 384345-29-3P 384345-30-6P 384345-31-7P 384345-32-8P 384345-33-9P 384345-34-0P 384345-35-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT 6066-82-6, N-Hydroxysuccinimide 14091-08-8, D-p-Chlorophenylalanine 78879-20-6, N-Boc-L-Tic-OH 115962-35-1, N-Boc-D-Tic-OH 193274-04-3, 3a-Benzyl-2-methyl-2,3a,4,5,6,7-hexahydropyrazolo[4,3-c]pyridin-3-one 218952-63-7, 8a-(Pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)tetrahydroimidazo[1,5-a]pyrazine-1,3-dione
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

L20 ANSWER 7 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:15253 CA
TITLE: **Melanocortin** receptor agonists, and preparation thereof, for therapeutic use
INVENTOR(S): Bakshi, Raman Kumar; Nargund, Ravi P.; Ye, Zhixiong
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001091752	A1	20011206	WO 2001-US17014	20010525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002004512	A1	20020110	US 2001-867309	20010529

US 6376509 B2 20020423
PRIORITY APPLN. INFO.: US 2000-207918P P 20000530
OTHER SOURCE(S): MARPAT 136:15253
GI



I

AB The invention discloses compds. and derivs. thereof which are agonists of the human **melanocortin** receptor(s) and, in particular, are selective agonists of the human **melanocortin**-4 receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, e.g. obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. Prepn. of e.g. I is described.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Melanocortin** receptor agonists, and preparation thereof, for therapeutic use

AB The invention discloses compds. and derivs. thereof which are agonists of the human **melanocortin** receptor(s) and, in particular, are selective agonists of the human **melanocortin**-4 receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, e.g. obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. Prepn. of e.g. I is described.

ST **melanocortin** 4 receptor agonist prepn therapeutic; obesity diabetes treatment **melanocortin** receptor agonist; **sexual dysfunction** treatment **melanocortin** receptor agonist; erectile dysfunction treatment **melanocortin** receptor agonist

IT Drug delivery systems
(capsules; **melanocortin** receptor agonist prepn. for therapeutic use)

IT Anticholesteremic agents
(cholesterol sequestrants; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)

IT Sexual behavior
(disorder; **melanocortin** receptor agonist prepn. for therapeutic use)

IT Sequestering agents
(for cholesterol; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
IT Sexual behavior
(impotence; **melanocortin** receptor agonist prepn. for therapeutic use)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** 4; **melanocortin** receptor agonist prepn. for therapeutic use)
IT Antidiabetic agents
Antiobesity agents
Drug delivery systems
(**melanocortin** receptor agonist prepn. for therapeutic use)
IT Dopamine agonists
(**melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
IT Sulfonylureas
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin**; **melanocortin** receptor agonist prepn. for therapeutic use)
IT Adrenoceptor antagonists
(.alpha.2-; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
IT Adrenoceptor agonists
(.beta.3-; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
IT 82785-45-3, Neuropeptide Y
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
IT 9001-42-7, .alpha.-Glucosidase 9028-35-7, HMG-CoA reductase 9068-52-4, Phosphodiesterase V
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
IT 378741-82-3P 379266-73-6DP, isomers 379266-73-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**melanocortin** receptor agonist prepn. for therapeutic use)
IT 378741-76-5 379266-96-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**melanocortin** receptor agonist prepn. for therapeutic use)
IT 59433-90-8P 378741-77-6P 378741-78-7P 378741-79-8P 378741-80-1P 379266-72-5DP, isomers 379266-72-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; **melanocortin** receptor agonist prepn. for therapeutic use)
IT 447-53-0, 1,2-Dihydronaphthalene 1189-71-5, Chlorosulfonyl isocyanate 24424-99-5 57292-44-1 115962-35-1 193274-04-3 378741-81-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; **melanocortin** receptor agonist prepn. for

therapeutic use)
IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sensitizers and mimetics; **melanocortin** receptor agonist
prepn. for therapeutic use, and use with other agents)

L20 ANSWER 8 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 135:314399 CA
TITLE: Detection of variations in the DNA methylation profile of genes in the determining the risk of disease
INVENTOR(S): Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander
PATENT ASSIGNEE(S): Epigenomics A.-G., Germany
SOURCE: PCT Int. Appl., 636 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 68
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077373	A2	20011018	WO 2001-DE1486	20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10019058	A1	20011220	DE 2000-10019058	20000406
WO 2001077373	A2	20011018	WO 2001-XA1486	20010406
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG				
WO 2001077373	A2	20011018	WO 2001-XB1486	20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG				
WO 2001077373	A2	20011018	WO 2001-XC1486	20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2000-10019058 A 20000406
WO 2001-DE1486 W 20010406

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the DNA methylation of a target group of genes. The invention further relates to the use of the same for detg. the gene variant with regard to DNA methylation, a medical device, using an oligonucleotide kit, a method for detg. the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a disease state in an individual. Such diseases may be: undesired pharmaceutical side-effects; cancerous diseases; CNS dysfunctions, injuries or diseases; aggressive symptoms or relational disturbances; clin., psychol. and social consequences of brain injury; psychotic disorders and personality disorders; dementia and/or assocd. syndromes; cardiovascular disease, dysfunction and damage; dysfunction, damage or disease of the gastrointestinal tract; dysfunction, damage or disease of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; dysfunction, damage or disease of the body as an abnormal development process; dysfunction, damage or disease of the skin, muscle, connective tissue or bones; endocrine and metabolic dysfunction, damage or disease; headaches or **sexual dysfunction**. This abstr. record is one of several records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the DNA methylation of a target group of genes. The invention further relates to the use of the same for detg. the gene variant with regard to DNA methylation, a medical device, using an oligonucleotide kit, a method for detg. the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a disease state in an individual. Such diseases may be: undesired pharmaceutical side-effects; cancerous diseases; CNS dysfunctions, injuries or diseases; aggressive symptoms or relational disturbances; clin., psychol. and social consequences of brain injury; psychotic disorders and personality disorders; dementia and/or assocd. syndromes; cardiovascular disease, dysfunction and damage; dysfunction, damage or disease of the gastrointestinal tract; dysfunction, damage or disease of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; dysfunction, damage or disease of the body as an abnormal development process; dysfunction, damage or disease of the skin, muscle, connective tissue or bones; endocrine and metabolic dysfunction, damage or disease; headaches or **sexual dysfunction**. This abstr. record is one of several records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** 4, detection of methylation in gene for; detection of variations in DNA methylation profile of genes in detg. risk of disease)

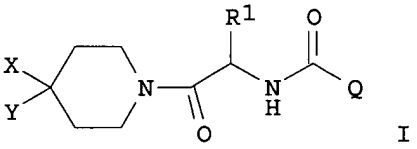
L20 ANSWER 9 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 135:272990 CA
TITLE: Preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists
INVENTOR(S): Palucki, Brenda L.; Barakat, Khaled J.; Guo, Liangqin; Lai, Yingjie; Nargund, Ravi P.; Park, Min K.; Pollard, Patrick G.; Sebhat, Iyassu K.; Ye, Zhixiong

PATENT ASSIGNEE(S): Merck + Co., Inc., USA
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070708	A1	20010927	WO 2001-US8935	20010320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002019523	A1	20020214	US 2001-812965	20010320

PRIORITY APPLN. INFO.: US 2000-191442P P 20000323
US 2000-242265P P 20001020

OTHER SOURCE(S): MARPAT 135:272990
GI



I

AB Title compds. [I; Q = (substituted) (fused) piperazinyl, morpholinyl, thiomorpholinyl; R1 = H, alkyl, (substituted) cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), etc.; X = (substituted) alkyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), heterocyclyl(alkyl), cyano(alkyl), aminosulfonyl(alkyl), etc.; Y = H, alkyl, cycloalkyl(alkyl), (substituted) aryl(alkyl), heterocyclyl(alkyl), heteroaryl(alkyl)], were prepd. as **melanocortin**-4 receptor (MC-4R) agonists. Thus, capsule formulations contg. title compd. (II) were prepd. Representative I activated MC-4R with IC50<1 .mu.M. I are claimed for the treatment of obesity, diabetes, and **sexual dysfunction** including erectile dysfunction and female **sexual dysfunction**.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists

AB Title compds. [I; Q = (substituted) (fused) piperazinyl, morpholinyl, thiomorpholinyl; R1 = H, alkyl, (substituted) cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), etc.; X = (substituted) alkyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), heterocyclyl(alkyl), cyano(alkyl), aminosulfonyl(alkyl), etc.; Y = H, alkyl, cycloalkyl(alkyl), (substituted) aryl(alkyl), heterocyclyl(alkyl), heteroaryl(alkyl)], were prepd. as **melanocortin**-4 receptor (MC-4R) agonists. Thus, capsule formulations contg. title compd. (II) were prepd. Representative

I activated MC-4R with IC50<1 .mu.M. I are claimed for the treatment of obesity, diabetes, and **sexual dysfunction** including erectile dysfunction and female **sexual dysfunction**.

ST piperazinylcarbonylaminomethylcarbonylpiperidine prepn **melanocortin** receptor agonist; **sexual dysfunction** treatment piperazinylcarbonylaminomethylcarbonylpiperidine; obesity treatment piperazinylcarbonylaminomethylcarbonylpiperidine; diabetes treatment piperazinylcarbonylaminomethylcarbonylpiperidine; piperidine piperazinylcarbonylaminomethylcarbonyl prepn **melanocortin** receptor agonist

IT Dopamine agonists
(combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Sulfonylureas
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Sexual behavior
(disorder, treatment; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Sexual behavior
(impotence, treatment; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Pituitary hormone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(**melanocortin** 4, agonists; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Antidiabetic agents
Antiobesity agents
(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Adrenoceptor antagonists
(.alpha.2-, combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Adrenoceptor agonists
(.beta.3-, combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT 171596-29-5, IC-351 171599-83-0, Sildenafil citrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT 363187-87-5P 363189-64-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT 363187-28-4P 363187-29-5P 363187-30-8P 363187-31-9P 363187-32-0P
363187-33-1P 363187-34-2P 363187-35-3P 363187-36-4P 363187-37-5P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT 363190-17-4P 363190-19-6P 363190-59-4P 363190-60-7P 363190-61-8P
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363620-36-4P 363620-38-6P 363620-40-0P 363620-41-1P 363620-43-3P
363620-45-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT 75-44-5, Phosgene 75-64-9, tert-Butylamine, reactions 95-89-6, 3-Chloro-2,5-dimethylpyrazine 110-85-0, Piperazine, reactions 124-68-5 535-11-5, Ethyl 2-bromopropionate 556-82-1, 3-Methyl-2-buten-1-ol 565-69-5, Ethyl isopropyl ketone 598-21-0 811-93-8, 1,2-Diamino-2-methylpropane 1067-74-9, Methyl diethylphosphonoacetate 1193-18-6 1436-59-5, cis-1,2-Diaminocyclohexane 2749-11-3, (S)-2-Amino-1-propanol 3674-13-3, Ethyl 2,3-dibromopropionate 5521-55-1, 5-Methyl-2-pyrazinecarboxylic acid 5521-61-9, 6-Methyl-2-pyrazinecarboxylic acid 6294-40-2 7051-34-5, Cyclopropylmethyl bromide 7764-95-6 10316-79-7 20607-43-6, Sodium isopropylsulfide 22059-21-8, 1-Aminocyclopropane-1-carboxylic acid 29460-90-0, 2-Isopropylpyrazine 35761-26-3 45767-66-6, 2-Chloro-4-fluorobenzyl bromide 57292-44-1 57292-45-2 62234-36-0 69555-14-2 83949-32-0 84358-13-4 92329-61-8 129799-15-1 138775-02-7 138775-03-8 139631-62-2, Cyclopropylsulfonyl chloride 142851-03-4 312638-87-2 363192-22-7 363192-64-7 363192-65-8 363192-66-9 363192-73-8 363192-76-1 363192-79-4 363192-81-8 363192-86-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT 2435-46-3P 19967-55-6P 29924-70-7P 35761-27-4P 96136-12-8P
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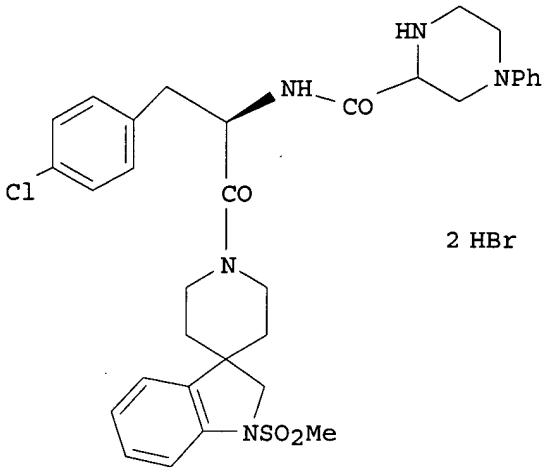
363192-61-4P 363192-62-5P 363192-63-6P 363192-67-0P 363192-68-1P
363620-42-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

L20 ANSWER 10 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 135:267270 CA
TITLE: Spiropiperidine derivatives as **melanocortin** receptor agonists
INVENTOR(S): Palucki, Brenda L.; Nargund, Ravi P.
PATENT ASSIGNEE(S): Merck + Co., Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070337	A1	20010927	WO 2001-US8833	20010320

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-191669P P 20000323
OTHER SOURCE(S): MARPAT 135:267270
GI



I

AB Certain novel spiropiperidine derivs. are agonists of the human **melanocortin** receptor(s) and, in particular, are selective agonists of the human **melanocortin**-4 receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. I was prepd. and pharmacol. tests are described.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Spiropiperidine derivatives as **melanocortin** receptor agonists

AB Certain novel spiropiperidine derivs. are agonists of the human **melanocortin** receptor(s) and, in particular, are selective agonists of the human **melanocortin**-4 receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. I was prepd. and pharmacol. tests are described.

ST spiropiperidine deriv prepn **melanocortin** receptor agonist

IT Sexual behavior
(disorder; spiropiperidine derivs. as **melanocortin** receptor agonists)

IT Sexual behavior
(impotence; spiropiperidine derivs. as **melanocortin** receptor agonists)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin**; spiropiperidine derivs. as **melanocortin** receptor agonists)

IT Antidiabetic agents
Antiobesity agents
(spiropiperidine derivs. as **melanocortin** receptor agonists)

IT 128908-32-7, **Melanocortin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(spiropiperidine derivs. as **melanocortin** receptor agonists)

IT 126937-41-5 138775-03-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(spiropiperidine derivs. as **melanocortin** receptor agonists)

IT 126937-42-6P 126937-43-7P 362513-36-8DP, acyl derivs. 362513-73-3P
362513-74-4P 362513-76-6P 362513-77-7P 362513-79-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(spiropiperidine derivs. as **melanocortin** receptor agonists)
IT 362513-35-7P 362513-36-8P 362513-37-9P 362513-38-0P 362513-39-1P
362513-40-4P 362513-41-5P 362513-42-6P 362513-43-7P 362513-44-8P
362513-45-9P 362513-46-0P 362513-47-1P 362513-48-2P 362513-49-3P
362513-50-6P 362513-51-7P 362513-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(spiropiperidine derivs. as **melanocortin** receptor agonists)
IT 362513-53-9P 362513-54-0P 362513-55-1P 362513-56-2P 362513-57-3P
362513-58-4P 362513-59-5P 362513-60-8P 362513-61-9P 362513-62-0P
362513-63-1P 362513-64-2P 362513-65-3P 362513-66-4P 362513-67-5P
362513-68-6P 362513-69-7P 362513-70-0P 362513-71-1P 362513-72-2P
362513-78-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(spiropiperidine derivs. as **melanocortin** receptor agonists)

L20 ANSWER 11 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 135:205579 CA
TITLE: HP-3228 and related peptides to treat **sexual dysfunction**
INVENTOR(S): Girten, Beverly E.; Tuttle, Ronald R.
PATENT ASSIGNEE(S): Lion Bioscience A.-G., Germany
SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 306,686.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6284735	B1	20010904	US 1999-356386	19990716
US 6127381	A	20001003	US 1999-301391	19990428
WO 2001005401	A1	20010125	WO 2000-US19408	20000713

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 1998-83368P P 19980428
US 1999-301391 A1 19990428
US 1999-306686 A2 19990506
US 1999-356386 A2 19990716
US 1999-364825 A2 19990730
US 1999-401004 A2 19990921

OTHER SOURCE(S): MARPAT 135:205579
AB Methods for treating erectile dysfunction in males and **sexual dysfunction**, such as sexual arousal disorder, in females. The methods involve administering an effective amt. of certain compds. such as

HP-228 (Ac-Nle-Gln-His(D)Phe-Arg-(D)Trp-Gly-NH2).
REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI HP-3228 and related peptides to treat **sexual dysfunction**
AB Methods for treating erectile dysfunction in males and **sexual dysfunction**, such as sexual arousal disorder, in females. The methods involve administering an effective amt. of certain compds. such as HP-228 (Ac-Nle-Gln-His(D)Phe-Arg-(D)Trp-Gly-NH2).
ST peptide HP228 **sexual dysfunction melanocortin** antagonist; erectile dysfunction peptide HP228 **melanocortin** receptor
IT Sexual behavior
(disorder; HP-3228 and related peptides to treat **sexual dysfunction**)
IT Sexual behavior
(impotence; HP-3228 and related peptides to treat **sexual dysfunction**)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** 3; HP-3228 and related peptides to treat **sexual dysfunction**)
IT 172617-89-9P, HP-228
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(HP-3228 and related peptides to treat **sexual dysfunction**)
IT 7565-89-1 170103-02-3 170103-04-5 182687-57-6 182687-58-7
182687-61-2 205499-42-9 205499-43-0 223473-41-4, HP 467
252047-01-1 252047-02-2 252047-03-3 252047-04-4 252047-05-5
252047-06-6 252047-07-7 252047-08-8 252047-09-9 252047-10-2
252047-11-3 252047-12-4 252047-13-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HP-3228 and related peptides to treat **sexual dysfunction**)
IT 128908-32-7, **Melanocortin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HP-3228 and related peptides to treat **sexual dysfunction**)

L20 ANSWER 12 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 135:175427 CA
TITLE: Uses of agrp-**melanocortin** receptor binding modulating compounds
INVENTOR(S): Hadcock, John Richard Neville; Swick, Andrew Gordon
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1125579	A2	20010822	EP 2001-300233	20010111

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO
US 2002065277 A1 20020530 US 2001-761320 20010116
BR 2001000106 A 20010828 BR 2001-106 20010118
JP 2001242173 A2 20010907 JP 2001-9643 20010118
PRIORITY APPLN. INFO.: US 2000-176508P P 20000118
US 2000-206126P P 20000522

AB The present invention provides a method of treating obesity, **sexual dysfunction** (including erectile dysfunction), diabetes, insulin resistance, hyperinsulinemia, Syndrome X, adrenal dysfunction, hypertension, hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia, or substance abuse, the method comprising the step of administering to a patent having or at risk of having one of the above-mentioned diseases a therapeutically effective amt. of a compd. that attenuates the binding of agouti-related protein to **melanocortin** receptors, but does not attenuate the binding of .alpha.-MSH to **melanocortin** receptors. The present invention also provides a method of identifying a compd. that is useful for the treatment or prevention of obesity, **sexual dysfunction** (including erectile dysfunction), diabetes, insulin resistance, hyperinsulinemia, Syndrome X, adrenal dysfunction, hypertension, hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia, or substance abuse, the method comprising the steps of: (1) detg. if a compd. affects the binding of agouti-related protein to **melanocortin** receptors; (2) detg. if a compd. affects the binding of .alpha.-MSH to **melanocortin** receptors; and (3) selecting a compd. that attenuates the binding of agouti-related protein to **melanocortin** receptors, but does not affect the binding of .alpha.-MSH to **melanocortin** receptors.

TI Uses of agrp-**melanocortin** receptor binding modulating compounds

AB The present invention provides a method of treating obesity, **sexual dysfunction** (including erectile dysfunction), diabetes, insulin resistance, hyperinsulinemia, Syndrome X, adrenal dysfunction, hypertension, hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia, or substance abuse, the method comprising the step of administering to a patent having or at risk of having one of the above-mentioned diseases a therapeutically effective amt. of a compd. that attenuates the binding of agouti-related protein to **melanocortin** receptors, but does not attenuate the binding of .alpha.-MSH to **melanocortin** receptors. The present invention also provides a method of identifying a compd. that is useful for the treatment or prevention of obesity, **sexual dysfunction** (including erectile dysfunction), diabetes, insulin resistance, hyperinsulinemia, Syndrome X, adrenal dysfunction, hypertension, hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia, or substance abuse, the method comprising the steps of: (1) detg. if a compd. affects the binding of agouti-related protein to **melanocortin** receptors; (2) detg. if a compd. affects the binding of .alpha.-MSH to **melanocortin** receptors; and (3) selecting a compd. that attenuates the binding of agouti-related protein to **melanocortin** receptors, but does not affect the binding of .alpha.-MSH to **melanocortin** receptors.

ST agouti related protein **melanocortin** receptor binding modulator

IT Drugs of abuse
(abuse of, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(agouti-related; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Antiarteriosclerotics
(antiatherosclerotics; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Sexual behavior
(disorder, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Lipoproteins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(hyperlipoproteinemia, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Sexual behavior
(impotence, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Radiochemical analysis
(in drug screening; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Pituitary hormone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**melanocortin** 3; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Pituitary hormone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**melanocortin** 4; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Pituitary hormone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**melanocortin**; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Diabetes mellitus
(non-insulin-dependent, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Disease, animal
(syndrome X, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with

melanocortin receptor agonists and other agents)

IT Anticholesteremic agents
Antidiabetic agents
Antihypertensives
Antiobesity agents
Drug delivery systems
Drug interactions
Drug screening
(therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Adrenal gland, disease
Alcoholism
Hypertriglyceridemia
(treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT 9004-10-8, Insulin, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(hyperinsulinemia and resistance, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with other agents)

IT 37213-49-3, .alpha.-MSH
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

L20 ANSWER 13 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 134:116238 CA
TITLE: **Melanocortin** receptor-3 ligands to treat **sexual dysfunction**
INVENTOR(S): Dines, Kevin C.; Gahman, Timothy C.; Girten, Beverly E.; Hitchin, Douglas L.; Holme, Kevin R.; Lang, Hengyuan; Slivka, Sandra R.; Watson-Straughan, Karen J.; Tuttle, Ronald R.; Pei, Yazhong
PATENT ASSIGNEE(S): Trega Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005401	A1	20010125	WO 2000-US19408	20000713

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6284735 B1 20010904 US 1999-356386 19990716

PRIORITY APPLN. INFO.: US 1999-356386 A2 19990716
US 1999-364825 A2 19990730
US 1999-401004 A2 19990921
US 1998-83368P P 19980428
US 1999-301391 A1 19990428
US 1999-306686 A2 19990506

OTHER SOURCE(S): MARPAT 134:116238

AB Methods for treating **sexual dysfunction**, such as erectile dysfunction or sexual arousal disorder, with a compd. having the generic formula X1-X2-D-Phe-Arg-D-Trp-X3 [X1 = R1R2NCHR3CY1Y2, Ac, H, or absent, where R1 = R2, COPh, CO2Bu-t, CO2CH2Ph, CHCO-(polyethylene glycol) or A which is N,O-(un)substituted 3-amino-4,5,6-trihydroxytetrahydro-2-pyranyl; R2 = H, Ac, Et, PhCH2; R3 = alkyl, cycloalkyl; Y1, Y2 = H or together form carbonyl or thiocarbonyl; X2 = NR1CHR4CY1Y2-His, His, Ac, or H, where R4 = (CH2)mCONH2, (CH2)mCONHR1, or (CH2)CONHA (m = 1-3); X3 = NR1CHR6(CH2)nCY1Y2R5 or R5, where R5 = OH, OR3, NH2, SH, NHMe, NHCH2PH, or A; R6 = H or R3, n = 0-3]. A particularly useful compd. is HP-228, which has the formula Ac-Nle-Gln-His-D-Phe-Arg-D-Trp-Gly-NH2. The invention also provides methods for selecting **melanocortin** receptor-3 ligands by detg. whether a compd. modulates the activity of MC-3 as an agonist or antagonist. These methods can be used to screen compd. libraries, including benzimidazoles, for ligands to treat MC-3-assocd. conditions. Such conditions include **sexual dysfunction**, including erectile dysfunction and sexual arousal disorder (data given).

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Melanocortin** receptor-3 ligands to treat **sexual dysfunction**

AB Methods for treating **sexual dysfunction**, such as erectile dysfunction or sexual arousal disorder, with a compd. having the generic formula X1-X2-D-Phe-Arg-D-Trp-X3 [X1 = R1R2NCHR3CY1Y2, Ac, H, or absent, where R1 = R2, COPh, CO2Bu-t, CO2CH2Ph, CHCO-(polyethylene glycol) or A which is N,O-(un)substituted 3-amino-4,5,6-trihydroxytetrahydro-2-pyranyl; R2 = H, Ac, Et, PhCH2; R3 = alkyl, cycloalkyl; Y1, Y2 = H or together form carbonyl or thiocarbonyl; X2 = NR1CHR4CY1Y2-His, His, Ac, or H, where R4 = (CH2)mCONH2, (CH2)mCONHR1, or (CH2)CONHA (m = 1-3); X3 = NR1CHR6(CH2)nCY1Y2R5 or R5, where R5 = OH, OR3, NH2, SH, NHMe, NHCH2PH, or A; R6 = H or R3, n = 0-3]. A particularly useful compd. is HP-228, which has the formula Ac-Nle-Gln-His-D-Phe-Arg-D-Trp-Gly-NH2. The invention also provides methods for selecting **melanocortin** receptor-3 ligands by detg. whether a compd. modulates the activity of MC-3 as an agonist or antagonist. These methods can be used to screen compd. libraries, including benzimidazoles, for ligands to treat MC-3-assocd. conditions. Such conditions include **sexual dysfunction**, including erectile dysfunction and sexual arousal disorder (data given).

ST peptide prepn **melanocortin** receptor **sexual dysfunction**; benzimidazole combinatorial library **melanocortin** receptor **sexual dysfunction**

IT Sexual behavior
(disorder; **melanocortin** receptor-3 ligands to treat **sexual dysfunction**)

IT Combinatorial library
(**melanocortin** receptor-3 ligands to treat **sexual dysfunction**)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(**melanocortin** receptor-3 ligands to treat **sexual dysfunction**)

IT Pituitary hormone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**melanocortin**; **melanocortin** receptor-3 ligands to treat **sexual dysfunction**)

IT 172617-89-9P, Hp-228
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**melanocortin** receptor-3 ligands to treat **sexual dysfunction**)

IT 7565-89-1P 170103-02-3P 170103-04-5P 170103-05-6P 182687-55-4P
182687-56-5P 182687-57-6P 182687-58-7P 182687-59-8P 182687-60-1P
182687-61-2P 205499-42-9P 205499-43-0P 223473-41-4P, HP 467
252047-01-1P 252047-02-2P 252047-03-3P 252047-04-4P 252047-05-5P
252047-06-6P 252047-09-9P 252047-10-2P 252047-11-3P 252047-12-4P
252047-13-5P 321180-15-8P 321180-17-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**melanocortin** receptor-3 ligands to treat **sexual dysfunction**)

IT 248947-36-6 321180-43-2 321180-45-4 321180-47-6 321180-49-8
321180-51-2 321180-53-4 321180-55-6 321180-57-8 321180-59-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**melanocortin** receptor-3 ligands to treat **sexual dysfunction**)

L20 ANSWER 14 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 134:76409 CA
TITLE: Compositions and methods for treatment of **sexual dysfunction**
INVENTOR(S): Blood, Christine H.; Shadiack, Annette M.; Bernstein, Joanna K.; Herbert, Guy W.
PATENT ASSIGNEE(S): Palatin Technologies Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000224	A1	20010104	WO 2000-US18217	20000629

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 2000012200 A 20020326 BR 2000-12200 20000629
EP 1196184 A1 20020417 EP 2000-950283 20000629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1999-142346P P 19990629
US 2000-194987P P 20000405
US 2000-606501 A 20000628
WO 2000-US18217 W 20000629

AB Compns. and methods are provided for the treatment of **sexual dysfunctions** in mammals, such as erectile dysfunction and female **sexual dysfunction**. In one embodiment, a peptide-based compn. including the peptide sequence Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH is administered. Methods of administration include injection, oral, nasal and mucosal administration.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Compositions and methods for treatment of **sexual dysfunction**

AB Compns. and methods are provided for the treatment of **sexual dysfunctions** in mammals, such as erectile dysfunction and female **sexual dysfunction**. In one embodiment, a peptide-based compn. including the peptide sequence Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH is administered. Methods of administration include injection, oral, nasal and mucosal administration.

ST **sexual dysfunction melanocortin** analog peptide

IT Drug delivery systems
(buccal; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Sexual behavior
(disorder, female; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Sexual behavior
(impotence; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems
(inhalants; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems
(injections; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Pituitary hormone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**melanocortin**; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems
(mucosal; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems
(nasal; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems
(oral; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems
(topical; **melanocortin** analogs for treating **sexual dysfunctions**)

IT 4289-02-5 31008-44-3 189691-06-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**melanocortin** analogs for treating **sexual dysfunctions**)

L20 ANSWER 15 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 134:42445 CA
TITLE: Preparation of piperidine amino acid derivatives as **melanocortin**-4 receptor agonists
INVENTOR(S): Bakshi, Raman K.; Barakat, Khaled J.; Nargund, Ravi P.; Palucki, Brenda L.; Patchett, Arthur A.; Sebhat, Iyassu; Ye, Zhixiong; Van, Der Ploeg Leonardus H. T.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Van Der Ploeg, Leonardus H. T.
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000074679	A1	20001214	WO 2000-US14930	20000531
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1187614	A1	20020320	EP 2000-937961	20000531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6350760	B1	20020226	US 2000-585111	20000601

PRIORITY APPLN. INFO.: US 1999-137477P P 19990604
US 1999-169209P P 19991202
WO 2000-US14930 W 20000531
OTHER SOURCE(S): MARPAT 134:42445
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Piperidine derivs. I [R2C2 = aryl, 5- or 6-membered heteroaryl or heterocyclyl, 5- to 7-membered carbocyclyl, which may be substituted; L = (CRb2)m, where Rb = H, alkyl, (CH2)n-cycloalkyl or -aryl; m = 0-2, n = 0-3; X, Y = (CH2)0-2; Ra = H, alkyl, (CHRb)n-cycloalkyl, -aryl, -heteroaryl, -O(CHRb)naryl, which may be substituted; Re = H, alkyl, (CH2)n-aryl, -cycloalkyl, -heteroaryl, which may be substituted, acyl, sulfonyl, etc.; R1 = H, alkyl, (CH2)n-cycloalkyl, -aryl, -heteroaryl, -heterocyclyl; R2 = any group given for R1, CN, (CH2)n-carboxamido, -carboxy, -acylamino, sulfonylamino, -amino, etc.] were prepd. as agonists of the human **melanocortin** receptors, in particular, the human **melanocortin**-4 receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual**

dysfunction, including erectile dysfunction and female **sexual dysfunction**. Thus, II trifluoroacetate, prepd. by coupling of Et 1-(D-4-chlorophenylalanyl)-4-cyclohexyl-4-[(1,2,4-triazol-1-yl)methyl]piperidine trifluoroacetate (prepn. given) with N-tert-butoxycarbonyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Boc-D-Tic), was > 2,200-fold, > 10,000-fold, and > 580-fold selective for the human MC-4R over human MC-1R, MC-2R, and MC-3R, resp.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of piperidine amino acid derivatives as **melanocortin** -4 receptor agonists

AB Piperidine derivs. I [R2C2 = aryl, 5- or 6-membered heteroaryl or heterocyclyl, 5- to 7-membered carbocyclyl, which may be substituted; L = (CRb2)m, where Rb = H, alkyl, (CH2)n-cycloalkyl or -aryl; m = 0-2, n = 0-3; X, Y = (CH2)0-2; Ra = H, alkyl, (CHRb)n-cycloalkyl, -aryl, -heteroaryl, -O(CHRb)naryl, which may be substituted; Re = H, alkyl, (CH2)n-aryl, -cycloalkyl, -heteroaryl, which may be substituted, acyl, sulfonyl, etc.; R1 = H, alkyl, (CH2)n-cycloalkyl, -aryl, -heteroaryl, -heterocyclyl; R2 = any group given for R1, CN, (CH2)n-carboxamido, -carboxy, -acylamino, sulfonylamino, -amino, etc.] were prepd. as agonists of the human **melanocortin** receptors, in particular, the human **melanocortin**-4 receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. Thus, II trifluoroacetate, prepd. by coupling of Et 1-(D-4-chlorophenylalanyl)-4-cyclohexyl-4-[(1,2,4-triazol-1-yl)methyl]piperidine trifluoroacetate (prepn. given) with N-tert-butoxycarbonyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Boc-D-Tic), was > 2,200-fold, > 10,000-fold, and > 580-fold selective for the human MC-4R over human MC-1R, MC-2R, and MC-3R, resp.

ST piperidine amino acid prepn **melanocortin** receptor agonist

IT Sexual behavior
(disorder; prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT Sexual behavior
(impotence; prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT Pituitary hormone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**melanocortin** 4; prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT Antidiabetic agents
Antiobesity agents
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT Dopamine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT Adrenoceptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(.alpha.2; prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT Adrenoceptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.beta.3; prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT 312637-61-9P 312637-63-1P 312637-77-7P 312637-91-5P 312638-30-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT 312637-47-1P 312637-48-2P 312637-49-3P 312637-51-7P 312637-53-9P
312637-55-1P 312637-57-3P 312637-59-5P 312637-64-2P 312637-65-3P
312637-66-4P 312637-67-5P 312637-68-6P 312637-70-0P 312637-72-2P
312637-73-3P 312637-75-5P 312637-79-9P 312637-81-3P 312637-82-4P
312637-83-5P 312637-85-7P 312637-87-9P 312637-89-1P 312637-90-4P
312637-92-6P 312637-93-7P 312637-94-8P 312637-95-9P 312637-96-0P
312637-97-1P 312637-98-2P 312637-99-3P 312638-00-9P 312638-02-1P
312638-04-3P 312638-06-5P 312638-08-7P 312638-10-1P 312638-11-2P
312638-13-4P 312638-15-6P 312638-17-8P 312638-19-0P 312638-21-4P
312638-23-6P 312638-24-7P 312638-26-9P 312638-28-1P 312638-29-2P
312638-32-7P 312638-33-8P 312638-35-0P 312638-36-1P 312638-37-2P
312638-38-3P 312638-40-7P 312638-42-9P 312638-44-1P 312638-46-3P
312638-47-4P 312638-48-5P 312638-49-6P 312638-50-9P 312638-52-1P
312638-54-3P 312638-56-5P 312638-58-7P 312638-59-8P 312638-60-1P
312638-61-2P 312638-62-3P 312638-63-4P 312638-64-5P 312638-65-6P
312638-66-7P 312638-67-8P 312638-69-0P 312638-70-3P 312638-71-4P
312638-72-5P 312638-73-6P 312638-74-7P 312638-75-8P 312638-77-0P
312638-79-2P 312638-81-6P 312639-64-8P 312639-65-9P 312639-66-0P
312639-67-1P 312639-68-2P 312639-69-3P 312639-70-6P 312639-71-7P
312639-72-8P 312639-73-9P 312639-75-1P 312639-76-2P 312639-77-3P
312639-78-4P 312639-80-8P 312639-82-0P 312639-83-1P 312639-84-2P
312639-85-3P 312639-87-5P 312639-88-6P 312639-89-7P 312639-90-0P
312639-91-1P 312639-92-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT 57-88-5, Cholesterol, biological studies 9001-42-7, .alpha.-Glucosidase 9028-35-7, HMG-CoA reductase 82785-45-3, Neuropeptide y
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT 312639-52-4P 312639-53-5P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT 542-69-8, Butyl iodide 24465-45-0 29364-29-2, Sodium 2-methyl-2-propanethiolate 29943-42-8, Tetrahydro-4H-pyran-4-one 31637-11-3 41253-21-8, 1,2,4-Triazole sodium salt 57292-44-1 115962-35-1 136465-81-1 142851-03-4 150417-15-5 167262-68-2 207342-56-1 273378-16-8
RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT 10462-00-7P 115238-58-9P 142001-86-3P 158144-85-5P 188916-68-9P
225240-55-1P 252008-88-1P 312638-82-7P 312638-83-8P 312638-84-9P
312638-86-1P 312638-87-2P 312638-88-3P 312638-89-4P 312638-91-8P
312638-93-0P 312638-94-1P 312638-95-2P 312638-96-3P 312638-97-4P
312638-98-5P 312638-99-6P 312639-00-2P 312639-01-3P 312639-02-4P
312639-03-5P 312639-04-6P 312639-06-8P 312639-08-0P 312639-09-1P
312639-11-5P 312639-12-6P 312639-13-7P 312639-14-8P 312639-15-9P
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312639-21-7P 312639-22-8P 312639-23-9P 312639-24-0P 312639-25-1P
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312639-31-9P 312639-32-0P 312639-33-1P 312639-34-2P 312639-35-3P
312639-36-4P 312639-37-5P 312639-38-6P 312639-39-7P 312639-40-0P
312639-41-1P 312639-42-2P 312639-43-3P 312639-44-4P 312639-45-5P
312639-46-6P 312639-47-7P 312639-48-8P 312639-49-9P 312639-50-2P
312639-51-3P 312639-54-6P 312639-55-7P 312639-56-8P 312639-57-9P
312639-58-0P 312639-59-1P 312639-60-4P 312639-61-5P 312639-62-6P
312639-63-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT 9004-10-8D, Insulin, mimetic, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

IT 9025-82-5, Phosphodiesterase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type V cyclic-GMP-selective phosphodiesterase inhibitor; prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)

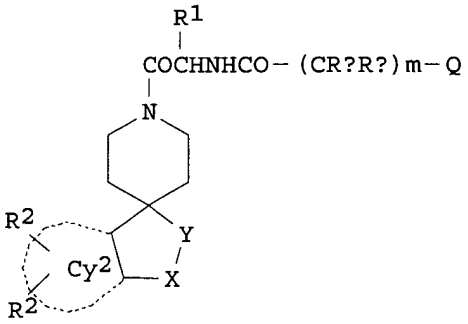
L20 ANSWER 16 OF 16 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 132:22957 CA
TITLE: Preparation of spiropiperidine derivatives as **melanocortin** receptor agonists
INVENTOR(S): Nargund, Ravi P.; Ye, Zhixiong; Palucki, Brenda L.; Bakshi, Raman K.; Patchett, Arthur A.; Van Der Ploeg, Leonardus H. T.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964002	A1	19991216	WO 1999-US13252	19990610
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9946801	A1	19991230	AU 1999-46801	19990610

AU 742425	B2	20020103				
EP 1085869	A1	20010328	EP 1999-930220		19990610	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO						
US 6294534	B1	20010925	US 1999-329814		19990610	
JP 2002517444	T2	20020618	JP 2000-553071		19990610	
US 2001029259	A1	20011011	US 2001-781373		20010212	
US 6410548	B2	20020625				
PRIORITY APPLN. INFO.:			US 1998-88908P	P	19980611	
			GB 1998-17179	A	19980806	
			US 1999-123260P	P	19990308	
			US 1999-329814	A3	19990610	
			WO 1999-US13252	W	19990610	

OTHER SOURCE(S): MARPAT 132:22957

GI



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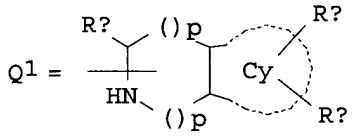

AB Certain novel spiropiperidine compds. I [Cy2 = six-membered arom. ring contg. 0 or 1 N; X = O, CH2, etc.; Q = Q1; Y = CO, SO2, etc; R1, Rb = H, C1-8 alkyl, etc.; R2 = H or halo; Rc = Rb, halo, ORb, NHSO2Rb, N(Rb)2, SO2Rb, CF3, OCF3; Cy = aryl, 5 or 6 membered heteroaryl, 5 or 6 membered heterocyclyl, 5 or 6 membered carbocyclyl; m, p, q independently = 0, 1, or 2] are agonists of **melanocortin** receptors (no data) and are useful for the treatment, control or prevention of diseases and disorders responsive to the activation of **melanocortin** receptors. The compds. of the present invention are therefore useful for treatment of diseases and disorders such as obesity, diabetes, **sexual dysfunction** including erectile dysfunction and female **sexual dysfunction**.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of spiropiperidine derivatives as **melanocortin**

receptor agonists

AB Certain novel spiropiperidine compds. I [Cy2 = six-membered arom. ring contg. 0 or 1 N; X = O, CH2, etc.; Q = Q1; Y = CO, SO2, etc; R1, Rb = H, C1-8 alkyl, etc.; R2 = H or halo; Rc = Rb, halo, ORb, NHSO2Rb, N(Rb)2, SO2Rb, CF3, OCF3; Cy = aryl, 5 or 6 membered heteroaryl, 5 or 6 membered heterocyclyl, 5 or 6 membered carbocyclyl; m, p, q independently = 0, 1, or 2] are agonists of **melanocortin** receptors (no data) and are useful for the treatment, control or prevention of diseases and disorders responsive to the activation of **melanocortin** receptors. The compds. of the present invention are therefore useful for treatment of diseases and disorders such as obesity, diabetes, **sexual dysfunction** including erectile dysfunction and female **sexual dysfunction**.

ST spiropiperidone prepn **melanocortin** receptor agonist; obesity treatment spiropiperidone; diabetes treatment spiropiperidone; **sex dysfunction** treatment spiropiperidone

IT Pituitary hormone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**melanocortin**; prepn. of and effect of spiropiperidine derivs.)

IT 252008-17-6P 252008-18-7P 252008-19-8P 252008-20-1P 252008-21-2P
252008-23-4P 252008-24-5P 252008-25-6P 252008-26-7P 252008-27-8P
252008-28-9P 252008-29-0P 252008-31-4P 252008-33-6P 252008-35-8P
252008-37-0P 252008-38-1P 252008-39-2P 252008-40-5P 252008-41-6P
252008-42-7P 252008-43-8P 252008-44-9P 252008-45-0P 252008-46-1P
252008-47-2P 252008-48-3P 252008-49-4P 252008-50-7P 252008-51-8P
252008-52-9P 252008-53-0P 252008-54-1P 252008-55-2P 252008-56-3P
252008-57-4P 252008-58-5P 252008-60-9P 252008-61-0P 252008-62-1P
252008-63-2P 252008-64-3P 252008-65-4P 252008-66-5P 252008-67-6P
252008-68-7P 252008-69-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiropiperidine derivs. as **melanocortin** receptor agonists)

IT 109-02-4, N-Methylmorpholine 2592-95-2, 1-Hydroxybenzotriazole
2627-86-3 3886-69-9 24424-99-5, Di-tert-butyl dicarbonate
40949-94-8, Potassium bis(trimethylsilyl)amide 57292-44-1 70601-64-8
78879-20-6 101752-05-0 115962-35-1 132705-51-2 134166-72-6,
D-4-Chlorophenylalanine methyl ester 136465-81-1 137419-24-0
142335-42-0 159634-86-3 252008-90-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of spiropiperidine derivs. as **melanocortin** receptor agonists)

IT 115238-59-0P 159634-59-0P 185526-14-1P 185526-28-7P 185526-32-3P
185526-40-3P 185526-41-4P 252008-70-1P 252008-71-2P 252008-72-3P
252008-73-4P 252008-74-5P 252008-75-6P 252008-76-7P 252008-77-8P
252008-78-9P 252008-79-0P 252008-80-3P 252008-81-4P 252008-82-5P
252008-83-6P 252008-84-7P 252008-85-8P 252008-86-9P 252008-87-0P
252008-89-2P 252008-91-6P 252008-92-7P 252008-93-8P 252008-94-9P
252008-95-0P 252008-96-1P 252008-97-2P 252008-98-3P 252008-99-4P
252009-00-0P 252009-01-1P 252009-02-2P 252009-03-3P 252009-04-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of spiropiperidine derivs. as **melanocortin** receptor agonists)

=> d his

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     (FILE 'HOME' ENTERED AT 10:41:47 ON 06 AUG 2002)

     FILE 'CA' ENTERED AT 10:41:55 ON 06 AUG 2002
L1            12 S MC-4R
L2          1327 S BIND (2A) SELECT?
L3         80191 S AGONIST
L4          6637 S MED OR (MALE ERECT? DYSFUN?)
L5             1 S L4 AND L2
L6            53 S L4 AND L3
L7            54 S L5 OR L6
L8            41 S L7 NOT PY>1999
L9            76 S MALE ERECT? DYSFUN?
L10          531 S SEX? DYSFUN?
L11          590 S L9 OR L10
L12          932 S MELANOCORTIN
L13           16 S L11 AND L12
L14            0 S L13 NOT PY>1999
L15        27472 S MC
L16       167019 S ME (2A) R
L17          266 S MC (2A) R
L18          148 S MC (2W) R
L19         1065 S L18 OR L12
L20           16 S L19 AND L11

=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y

STN INTERNATIONAL LOGOFF AT 10:50:17 ON 06 AUG 2002
```